Sleep and Wake Disorders Following Traumatic Brain Injury: Impact on Recovery of Cognition and Communication

by

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Abstract

Objective: To examine sleep and wake disorders following traumatic brain injury (TBI) and their impact on recovery of cognition, communication and mood. **Research Design:** This three-manuscript thesis comprises an introduction to sleep in the context of human function and development. It is followed by a systematic review of the literature pertaining to sleep and wake disorders following TBI, and then explores the relationship between sleep and arousal disturbance and functional recovery of cognitive-communication through a single case study, pre–post intervention. Finally, a larger study longitudinally explores the impact of treatment to optimize sleep and wakefulness on recovery of cognition, communication and mood through objective and subjective measures, pre-post intervention. The thesis concludes with a chapter that addresses the implications of findings for rehabilitation from the perspective of the International Classification of Functioning, Disability and Health (ICF), and a presentation of future research directions for the field **Methods:** The first manuscript involved a systematic review and rating of the quality of evidence. The second manuscript involved the evaluation of sleep and

wakefulness by objective measures, and longitudinally by self-report through the Daily Cognitive-Communication and Sleep Profile (DCCASP, © Wiseman-Hakes 2008, see Appendix S). Cognitive-communication abilities were also measured by the DCCASP. The third manuscript utilized a single case series and cohort design to evaluate sleep and wakefulness, and to examine cognition, communication and mood at baseline and following optimization of sleep and wakefulness. **Results:** For Manuscript One, 43 articles were reviewed for levels and quality of evidence across 5 domains: epidemiology, pathophysiology, neuropsychological implications, intervention and paediatrics. In Manuscript Two, we showed that there was a statistically and functionally significant relationship between perceived quality of sleep and language processing, attention and memory, seen across the phases of the intervention. In Manuscript Three, we showed that there were statistically and functionally significant improvements across several domains of cognition, communication and mood in response to treatment. **Conclusions:** Sleep and wake disorders after TBI are pervasive, and can negatively impact rehabilitation and recovery. There is a need for systematic evaluation and intervention for these disorders in all persons with TBI.

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Chapter 1
Introduction

1. Background

Traumatic brain injury (TBI), defined as an acquired, nondegenerative insult to the brain from an external mechanical force, is a leading cause of death and disability in both Canada and the United States, for both adults and children (World Health Organization [WHO], 2010). Brain Injuries are more common than breast cancer, spinal cord injury, HIV/AIDS and multiple sclerosis combined (Colantonio et al., in press). In the province of Ontario, 18,033 people sustained a TBI in 2007 and 2008, and nearly a ½ million live with a brain injury (Colantonio et al., 2010). TBI can result in significant impairments in physical, neurocognitive and psychosocial/emotional function, as well as impairments in communication and sleep. Regardless of injury severity, these impairments may be transient or permanent, resulting in profound disruption for survivors. It has been reported that the consequences of these impairments may endure across the life span, although their impact may vary depending on stage of recovery (O'Connor, Colantonio, & Polatajko, 2005).

Sleep and wake disorders such as insomnia, reduced arousal and excessive daytime sleepiness affect large proportions of individuals with traumatic brain injury (TBI) (Wiseman-Hakes, Gargaro, & Colantonio, 2009). A neglected field until recently, sleep-wake disturbance is becoming an increasingly important issue in the rehabilitation of patients with traumatic brain injury (TBI). These disorders are prevalent across all levels of severity and across the continuum of recovery, with reports of occurrence for many years post-injury. Studies conducted amongst heterogeneous samples of individuals with TBI report an incidence of sleep disorder that varies from 30-70% during the first 3 months post-injury and a prevalence up to 73% long past the injury (French & Parkinson, 2008); approximately 30% meet the DSM-IV criteria for insomnia (Beetar, Guilmette, & Sparadeo, 1996; Burke, Shah, Schneider, Ahangar, & Al-Aladai, 2004; Castriotta & Lai, 2001; Fichtenberg, Zafonte, Putnam, Mann, & Millard, 2002; Orff, Ayalon, & Drummond, 2009;

Ouellet, Beaulieu-Bonneau, & Morin, 2006; Ouellet, Savard, & Morin, 2004; Parcell, Ponsford, Rajaratnam, & Redman, 2006; Rao et al., 2008; Schreiber et al., 2008; Seyone & Kara, 2006; Defense and Veterans Brain Injury Center, 2009; Verma, Anand, & Verma, 2007; Williams, Lazic, & Ogilvie, 2008; Zeitzer, Friedman, & O'Hara, 2009). Although they are among the most commonly reported neuropsychiatric sequelae following TBI, the impact of these disorders on aspects of recovery has received limited scientific attention to date. Disturbances in sleep and wakefulness have been reported to exacerbate other trauma related disorders in cognition, communication, mood and pain, as well as compromise the rehabilitation process and community reintegration (Wiseman-Hakes, Victor, Brandys, & Murray, 2011). Still much research is needed to understand the etiology and evolution of these problems, their interrelationship with other aspects of recovery, and to develop effective treatments adapted to the complex reality of this population.

1.1 Introduction to Cognitive-Communication Disorders

Cognitive-communication disorders (CCDs) are the most prevalent group of communication disorders after TBI, with a reported incidence as high as 80-100% (Halper, Cherney, & Miller, 1991; Sarno, 1980; Sarno, Buonaguro, & Levita, 1986). "Cognitive-communication disorders encompass difficulties with any aspect of communication that is affected by disruptions of cognition. Communication includes listening, speaking, gesturing, reading and writing in all domains of language (phonologic, morphologic, syntactic, semantic and pragmatic). Cognition includes cognitive processes and systems (e.g., attention, memory, organization, executive functions). "Areas of function affected by cognitive impairments include behavioral self-regulation, social interaction, activities of daily living, learning and academic performance, and vocational performance" (American Speech-Language-Hearing Association, 2005, p. 1).

Cognitive-communication disorders are unique from other motor speech and specific language impairments such as aphasia, as they result from generalized cognitive and self-regulatory disturbance (Douglas, Bracy, & Snow, 2007; Heilman, Safran, & Geschwind, 1971; McDonald, 2003; Ylvisaker, 2006; Ylvisaker, Turkstra, & Coelho, 2005; Ylvisaker, Turkstra, et al., 2007). They have the greatest impact on communication at the level of

discourse and social exchange as opposed to speech sounds and words (Bigler, 1988; Halpern, Darley, & Brown, 1973; Hartley & Levin, 1990; Marquardt, Stoll, & Sussman, 1988; Rusk, Block, & Lowmann, 1969; Togher, McDonald, & Code, 1999). CCDs can have a negative impact across the continuum of recovery. Impaired communication can affect the rehabilitation process, social reintegration, community independence, family interactions, successful employment and academic success (Brookes, McKinlay, Symington, Beattie, & Campsie, 1987; Dahlberg et al., 2007; DePompei & Zarski, 1989; Douglas et al., 2007; Glang et al., 2008; Heilman et al., 1971; Larkins, 2007; Marquardt et al., 1988; McDonald & Togher, 2006; Ylvisaker, 2006; Ylvisaker, Adelson, et al., 2005; Ylvisaker et al., 2007). Thus, interventions that address cognitive-communication disorders either directly or indirectly, can help to improve outcomes such as quality of life for survivors (Bornhofen & McDonald, 2008; Cicerone et al., 2000; Dahlberg et al., 2007; Togher, McDonald, Code, & Grant, 2004).

Research has identified the following cognitive-communication disorders among individuals with TBI; impoverished, vague, tangential or disorganized discourse (oral and or written) (Coelho, 2002; Coelho, Grela, Corso, Gamble, & Fenn, 2005; Coelho, Ylvisaker, & Turkstra, 2005), impaired comprehension in the presence of length, complexity, detail, indirect content, (implied, abstract, figurative, humorous), background noise, multiple speakers, rapid presentation or rapid shifts from topic to topic (Docking, Jordan, & Murdoch, 1999; Moran, Nippold, & Gillon, 2006); word finding problems particularly in conversation or generative contexts (Jurado, Mataro, Verger, Bartumeaus, & Junque, 2000; King, Hough, Walker, Rastatter, & Holbert, 2006); pragmatic or social communication difficulties including problems related to initiation, turn-taking, topic management, conversational repair, self-monitoring, social perception and adaptation to the needs of the conversational partner and context, (Dahlberg et al., 2006; Douglas et al., 2007; Turkstra, 2003; Turkstra, McDonald, & DePompei, 2001), and difficulties using or communication to assist memory and new learning. Additionally, follow-up studies regarding the long-term consequences of TBI have identified that individuals across all levels of severity report symptoms of impaired attention and concentration 10 years post-injury. They also reported difficulties with expressive communication, and difficulties following and understanding conversations in both individual and group settings, as enduring disabilities

(O'Connor et al., 2005). Thus, the primary focus of interventions for these disorders is to maximize functional communication.

1.2 Introduction to Sleep Physiology

Sleep occupies between one quarter and one third of the average human life, and yet its' significance remains relatively misunderstood. This may be due in part, to the fact that it is defined not necessarily as a physiological state, but rather as an altered state of consciousness; that is,

> a behavioural state that alternates with waking, and relative to which, it is characterized by a heightened threshold to sensory input, attenuation of motor output, (with the exception of respiration and eye movements), characteristic changes in central and peripheral physiology, and diminished conscious awareness. (Stickgold & Walker, 2009, p. xiii)

Further,

> there is not one specific mechanistic pathway that controls the generation and or termination of sleep; it is regulated by a highly complex interaction of neurological and psychological mechanisms including the circadian rhythm of the suprachisamatic nucleus, to the frontal cortical arousal system, and psychological processes such as anxiety and depression. (Stickgold & Walker, 2009, p. xiii)

There are two major types of sleep characteristic of all mammals, which are referred to as rapid eye movement (REM) sleep and nonrapid eye movement (NREM) sleep. NREM sleep is divided into four stages. NREM and REM cycles alternate in regular time periods, and as such, are controlled by a regular oscillation. In adult human sleep, this period ranges from 90-120 minutes per cycle, with approximately 4-5 cycles per night (see Figure 1).

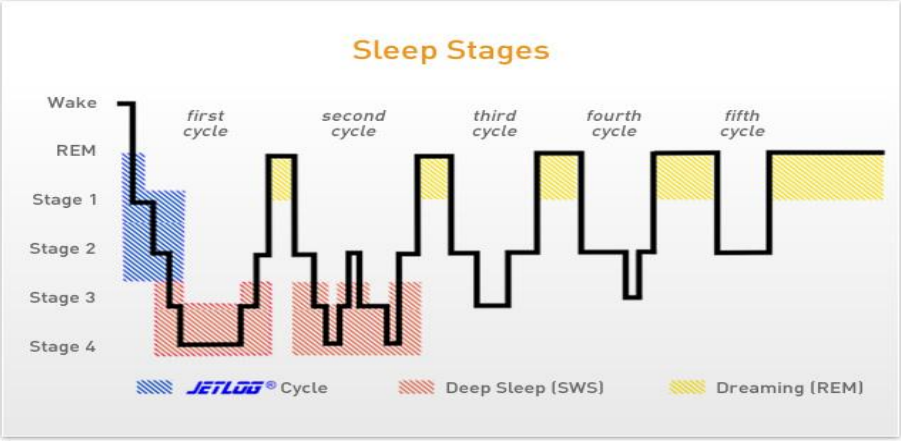

Figure 1. **Characteristic cycle of sleep stages (Retrieved from Google Images, 2011).**

Human sleep has a characteristic 'architecture' that is measured through polysomnographic recordings of EEG (electroencephalography, i.e., measurement of brain wave activity), EOG (electro-oculography, measurement of eye movements) and EMG (electromyography, measurement of muscle activity). Three terms characterize the EEG, and are important in the interpretation of wave patterns: frequency, amplitude and morphology. Frequency refers to "the rapidity of fluctuation in electrical potential between successive peaks or troughs of measured EEG brain waves, and are measured in cycles per second (Hertz/Hz)" (Pace-Schott, 2009, p. 11). Amplitude refers to "the magnitude of the electrical potential change between wave peaks and troughs, and is measured in microvolts" (Pace-Schott, 2009, p. 11). Finally, morphology refers to "the shape of a particular EEG wave (or group of waves), reflecting both their frequency and amplitude" (Pace-Schott, 2009, p. 11).

The gradual onset of NREM sleep is characterized by a slowing in frequency of brain waves from the beta and gamma frequencies which predominate during eye opening/waking, to alpha waves when the eyes close, and then to a predominance of theta waves during Stage 1 sleep. As sleep progresses in depth through NREM Stages 2-4, the wave patterns decrease in frequency and increase in amplitude. The Stage 2 EEG is also characterized by two distinctive wave forms, called spindles and K-Complexes. This latter form is particularly relevant when studying the sleep of those with TBI. Recent findings by Milner and Cote

(2009, 2010) report a decrease in K complexes in the sleep architecture of those with TBI in comparison to healthy controls. These findings may provide some explanation for the 'non- restful' quality of 'TBI sleep' as the threshold for external sensory input (i.e., sensory gating) is not reduced to the same degree as controls, consistent with an 'aging' brain. During Stage 3 sleep, the spindles decrease, the EEG frequency slows further and the amplitude increases to what is referred to as Stage 3-4 slow wave restorative sleep (SWS), characterized by the delta wave.

REM sleep, also known as 'paradoxical sleep', or 'active sleep', is the period during which the most vivid dreaming occurs. In contrast to NREM sleep, REM sleep is characterized by an EEG frequency similar to a waking EEG, and contains 'saw-tooth like waves', and is reflective of cortical activation by the cholinergic ascending arousal system. However, despite the cortical activation, muscle tone reaches its' minimum (resulting from central, brain stem-mediated inhibition of spinal alpha motor neurons), and known as REM 'atonia' (Carskadon & Dement, 2005).

Functional neuroimaging studies have revealed that NREM sleep is associated with widespread cortical deactivation (relative to waking) that is especially pronounced in the frontal cortex (Nofzinger, 2005). During REM however, midline limbic and paralimbic areas (associated with emotion and memory) are selectively activated, while much of the lateral cortex remains in the less activated state characteristic of NREM sleep (Nofzinger, 2005). Each sleep stage is characterized by its' own electrophysiological parameters including a unique EEG wave form (Chong, Sahlem, & Bazil, 2007) as shown in Figure 2.

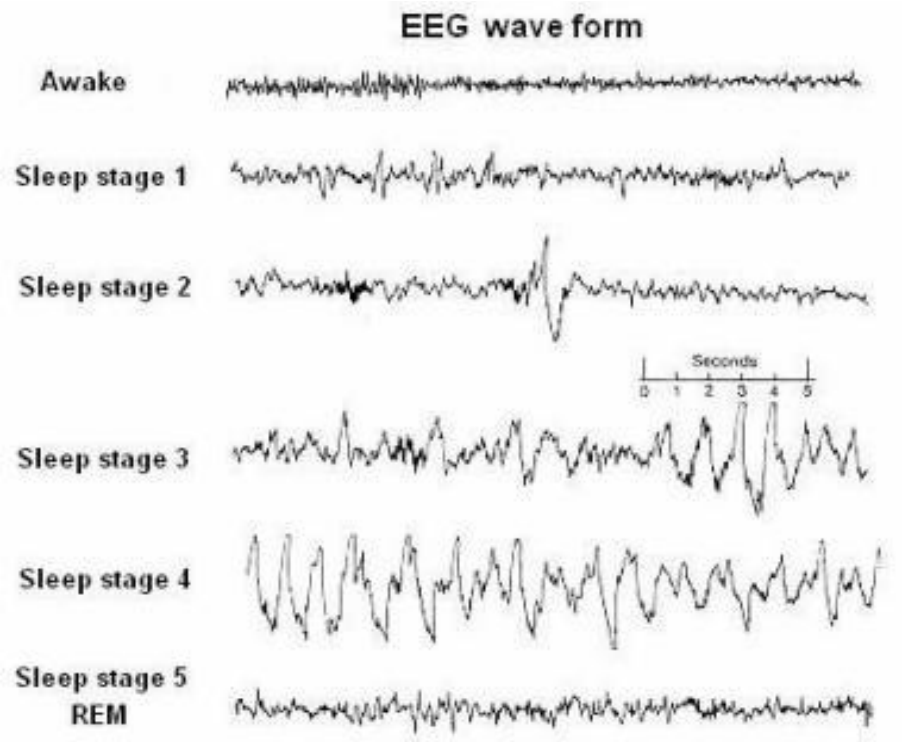

Figure 2. **Sleep architecture wave characteristics (Retrieved from Google Images, 2011).**

Of interest, healthy young adults between the ages of 20–40 years typically spend the following amounts of total NREM sleep time in various sleep stages (see Table 1):

Table 1

Percentage of Time Spent in Sleep Stages

Sleep Stage	Amount of time spent in each Stage (%)
Stage 1	2-5
Stage 2	45-55
Stage 3	3-8
Stage 4	10-15

1.3 Homeostatic and Circadian Control of Sleep Onset

The propensity for sleep is based on a two-process model proposed by Borbély and Achermann (2005), and first published by Borbély in 1982. This model is important to the understanding of sleep and wake disorders after TBI, as sleepiness and fatigue are often incorrectly referred to as being the same thing amongst this population, however, they are physiologically quite different. The Borbély model suggests that the transitions between sleep and wakefulness are controlled by the interaction of a homeostatic mechanism (Process S) and a circadian factor (Process C). Process S refers to an actual 'sleep drive' that builds throughout the day as a function of the duration spent in wakefulness, whereas Process C, refers to 'sleep propensity that varies as a function of time of day', and is an example of a physiological circadian rhythm whose 'master clock' resides in the suprachisamatic nucleus (SCN) of the anterior hypothalamus. Further, secretion of the sleep hormone melatonin from the pineal gland is also controlled by the SCN via a multi-synaptic pathway that provides an internal signal of circadian time, as well as feedback to the SCN via the melatonin receptors. Thus, if an individual is tired and actually 'sleepy', due to a build-up of Process S, they will in fact, fall asleep (or experience a drive to fall asleep) when they lie down or are in a quiet room with minimal stimulation (which is the premise of the MWT; Multiple Wake test, that will be described further in Chapter 5). In contrast, a person who is experiencing fatigue does not always experience simultaneous sleepiness. Fatigue may be experienced in isolation from sleepiness, in which case the individual will not have the same drive to fall asleep.

1.4 Introduction to and Definition of Fatigue

Like sleep and wake disorders, fatigue is also a commonly reported sequelae after TBI, with estimates of incidence reported by those in the community at 50-80% (Olver, Ponsford, & Curran, 1996). While the two are closely intertwined, they are often misinterpreted as being one and the same. However, fatigue in of itself, (particularly in this and other neurological populations) is a subjective experience, in contrast to sleepiness which has a physiological marker (Process S). Hypersomnia, or excessive sleepiness, is also common following TBI and often results in the individual falling asleep during the day, and/or in

situations where one would typically stay awake. Fatigue as defined in the medical literature is a "subjectively overwhelming sense of tiredness, lack of energy, and feeling of exhaustion, irrespective of sleep status" (Levine & Greenwald, 2009). Levine and Greenwald report that people with neurologic disorders including TBI, describe fatigue differently from the general population, in that 'neurologic fatigue' does not respond to sleep or rest, nor is it accompanied by the desire to sleep. There is also an important distinction between peripheral and central fatigue. Peripheral fatigue (or 'physical fatigue') is most often described by individuals as musculoskeletal symptoms that can impair mobility and ability to perform ADL's (activities of daily living). In contrast, central fatigue, also referred to as mental or cognitive fatigue, results from dysfunction of the supratentorial structures involved in performing cognitive tasks. Central fatigue is the predominant type of fatigue experienced by individuals with TBI, and is reflected by difficulties initiating and sustaining mental and physical tasks in the absence of motor impairments (Chaudhuri & Behan, 2000; Levine & Greenwald, 2009; Lou, Keams, Okan, Sexton, & Nutt, 2001). Impairments in the ability to maintain focused attention (vigilance) is a hallmark of central fatigue, as focused attention underlies the ability to process and integrate the mental, physical and sensory stimuli involved in task completion. Levine and Greenwald (2009) report that once focused attention is impaired, the ability to integrate the various types of information needed to complete a task becomes compromised and thus requires greater effort to complete.

1.5 Statement of the Problem

The link between sleep and cognition, and sleep and mood has been well documented in the literature (Giglio, Lane, Barkoukis, & Dumitru, 2007; Maquet, Smith, & Stickgold, 2003; Stickgold, 2003a, 2003b; Stickgold & Walker, 2007). As stated above, there are five stages of sleep, divided into NREM (Rapid eye movement) sleep (stages 1-4) and REM sleep. Studies of NREM and REM sleep, and the importance of their temporal succession in both animals and humans reveal that these stages have been found to play key roles in certain types of memory and learning, as well as cerebral plasticity (Giglio et al., 2007; Stickgold, 2003b; Walker, 2009). REM sleep, which occurs at the end of each sleep cycle, and the overall length of the REM cycle peaks, prior to wakening, also play a key role in memory

consolidation and new learning. Furthermore, REM sleep during the neonatal period plays an important role in brain growth, neuronal maturation, connectivity and synaptic plasticity in infants.

Studies are emerging that examine the lack of amounts of, or lack of restful sleep on human function. It has been reported that sleep deprivation impairs a wide range of functions, including endocrine function, immune regulation and metabolic control (Mullington, 2009), as well as neurocognitive processes such as learning and memory (Stickgold & Walker, 2009). Findings of a recent longitudinal study (average follow-up of 5.4 years) of 5431 healthy middle aged individuals (1459 F, 3972 M) found that changes in duration of sleep (both a decrease or increase from an average baseline of 6-8 hours per night, resulted in poorer cognitive function in comparison to those whose sleep patterns did not change from a baseline of 6-8 hours per night. These changes included impairments in reasoning, vocabulary, phonemic and semantic fluency and decrease in scores on the mini mental state examination (Ferrie et al., 2011). Further, a recent study examining the impact of sleep disturbance post-TBI on recovery of attention identified that those with TBI and poor sleep had significantly worse performance on measures of sustained attention than those with TBI and normal sleep (Bloomfield, Espie, & Evans, 2010). Sleep disturbances and reduced sleep have also been shown to have a negative impact on mood. Results of a neuroimaging study identified that just one night of consecutive sleep loss in a healthy population results in a hyper-limbic brain response to aversive stimuli or negatively aversive challenges, and that this 'amplified amygdala activity' is associated with a loss of top-down prefrontal control over emotional reactivity. The authors of this study reported that sleep appears to "reset" the correct emotional brain reactivity to next-day aversive challenges by maintaining functional integrity of this prefrontal-amygdala circuit (Yoo, Gujar, Hu, Jolesz, & Walker, 2007). These findings provide key insights into the pervasive relationship between sleep disruption and mood disorders, which are also prevalent following TBI. This study provides evidence to support that mood disorders (depression, lability, PTSD), which instead of being viewed as co-occurring with a sleep disorder, may in fact be more causally related (Yoo et al., 2007). Some initial research has looked at the relationship between sleep and cognition in survivors of TBI. Results of these studies

report greater impairments in sustained attention, memory, higher order executive functions and speed of information processing in patients with TBI and sleep disturbances in comparison to patients with TBI without sleep disturbances (Castriotta et al., 2009; Mahmood, Rapport, Hanks, & Fichtenberg, 2004; Makley et al., 2009; Wilde et al., 2007). This body of research emphasizes the crucial need for successful management of sleep/wake disturbances following TBI, in part to optimize the rehabilitation of cognition and resulting cognitive-communication impairments, thus potentially improving functional communication in survivors of TBI.

Despite the prevalence of sleep/wake and cognitive-communication disturbances post-trauma, the interrelationship between the two has received limited scientific attention to date

1.6 Rationale for Present Study

Given our understanding of the interrelationships between amount and quality of sleep, arousal and wakefulness, cognition and mood, it makes intuitive sense that impaired sleep after brain injury may have a negative impact on cognitive recovery, and may also exacerbate mood disturbances. This may further impact communication outcomes, given the underlying role that cognition plays in successful communication, and the fact that mood disturbances may cause withdrawal from situations requiring social communication. However, despite this knowledge and understanding, this study is the first of its kind to longitudinally examine the relationship between sleep and wake disorders and recovery of cognition and communication, and to qualitatively examine associated participation outcomes.

Further, despite the fact that literature on sleep and wake disorders after TBI is emerging, and there have been two review articles on the topic, there has been no systematic review of the literature. Thus, there is a need to examine the methodological quality of the evidence across the continuum of recovery, and to translate the evidence in a format that may support practice and ongoing research agendas.

1.7 Objectives

The main objectives of this thesis are:

1. To systematically appraise the literature relating to sleep and wake disorders associated with traumatic brain injury according to the following domains: epidemiology, pathophysiology, neuropsychological implications, paediatrics, and intervention.
2. To summarize the best evidence with a goal of knowledge translation to clinical practice and to provide recommendations as to how the field can best be advanced in the most scientifically rigorous manner.
3. To conduct a preliminary pilot case study examining the effects of a comprehensive, longitudinal approach to management of posttraumatic hypersomnia and mood disturbance using a newly developed self-report measure of functional cognitive, communication and mood status in a young adult with severe traumatic brain injury.
4. To conduct a pilot intervention study informed by the longitudinal case study to assess the impact of treatment for sleep/wake disorders on attention, speed and capacity of language processing, general neuropsychological status, anxiety, depression and communication, as well as qualitatively examining participation outcomes, using both self-report and objective measures.
5. To discuss the methodological issues and challenges of conducting real world sleep intervention research in a moderate to severe TBI adult population.

1.8 Roadmap of the Thesis

Chapter 1: Introduction and Objectives

Chapter 2: Manuscript One. Presentation of a systematic review of the literature pertaining to sleep and wake disorders after TBI, including evidence tables, practice points and research agenda.

Chapter 3: Manuscript Two. Introduction to the clinical relevance of careful assessment, monitoring and treatment for sleep and wake disturbances in a young adult with severe

traumatic brain injury in a single case study pre–post intervention design (study #1). This manuscript was the pilot work for Manuscript Three (chapter 4), and provided the basis for the design of the larger study (study #2, manuscript three). This manuscript also introduced the Daily Cognitive-communication and Sleep Profile, one of the measures used for study #2.

Chapter 4: Manuscript Three. A larger pilot intervention study (study #2) reporting the observed changes in cognition, communication and mood in response to optimization of sleep and wakefulness in twelve adults with traumatic brain injury.

Chapter 5: Conclusions

Chapter 2
Sleep and Wake Disorders Following Traumatic Brain Injury: A Systematic Review of the Literature[1]

2. Abstract

Background: Traumatic brain injury is a leading cause of death and disability in both Canada and the United States. Disorders of sleep and wakefulness are among the most commonly reported sequelae post-injury, across all levels of severity. Despite this, sleep and wakefulness are neither routinely, nor systematically, assessed and are only recently beginning to receive more clinical and scientific attention. **Objectives:** This review aims to systematically appraise the literature regarding sleep and wake disorders associated with traumatic brain injury according to the following domains: epidemiology, pathophysiology, neuropsychological implications, and intervention; to summarize the best evidence with a goal of knowledge translation to clinical practice; and to provide recommendations as to how the field can best be advanced in the most scientifically rigorous manner. **Methods:** Systematic review and rating of the quality of evidence. **Results:** Forty-three articles were reviewed for levels and quality of evidence. Fifty-six percent of the literature was classified as Level III, and 24% were Level IVA. Overall, 89% were rated as moderate quality. A separate summary was provided for the pediatric literature. **Conclusions:** A comprehensive review of the emerging literature revealed wide ranges in estimates for incidence and prevalence of sleep disorders following TBI depending on characteristics of patients, measures used, and length of follow-up. Few treatments have been found to be effective and as such more research is recommended. Our overview of the pediatric literature shows that this is an important issue for survivors of all ages. Overall, further work is needed to fully understand this complex disorder and to identify appropriate and timely interventions.

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[1] This chapter has previously been published: Wiseman-Hakes C., Colantonio, A., & Gargaro, J. (2009). Sleep and wake disorders following traumatic brain injury: A systematic review of the literature. *Critical Reviews in Physical and Rehabilitation Medicine, 21*(3–4), 317–374. Invited.

Key words: traumatic brain injury, mild traumatic brain injury, sport-related concussion, sleep, sleep disorders, insomnia, hypersomnia, excessive somnolescence, treatment

2.1 Background and Introduction

Traumatic brain injury (TBI), defined as an acquired nondegenerative, noncongenital insult to the brain from an external mechanical force, is a leading cause of death and disability in both Canada and the United States for both adults and children (WHO, 2010). Furthermore, although the literature reviewed in this paper is truly international in scope, at this time in the United States, "the nature of modern tactical engagement…in the current Iraq and Afghanistan conflicts has resulted in the largest proportion of identified traumatic brain injuries in any conflict in the nation's history" (French & Parkinson, 2008, p. 1004). In fact, the US Department of Defense reported an incidence of 10,963 diagnosed conflict-related TBIs in the year 2000. However this incidence was reported as 27,862 by December 31, 2009, which represents an increase of 145% (Defense and Veterans Brain Injury Center, 2009). TBI can result in significant impairments in physical, neurocognitive, and psychosocial/emotional function as well as impairments in communication and sleep. Regardless of injury severity, these impairments may be transient or permanent, resulting in profound disruption for survivors and their families.

Disorders of sleep and wakefulness are among the most commonly reported sequelae post-injury, across all levels of severity (Ouellet et al., 2006; Seyone & Kara, 2006). Despite this, sleep and wakefulness are neither routinely, nor systematically, assessed post-injury, and are only recently beginning to receive more clinical and scientific attention. Previous reviews by Ouellet et al. (2004), Orff et al. (2009), and most recently by Zeitzer et al. (2009), indicate that the field is still in a developmental stage and a body of literature is beginning to emerge. These previous reviews focused primarily on the prevalence and nature of sleep disorders and, to a lesser extent, on implications and effective treatment strategies among adult TBI survivors.

As of yet, there has been no systematic appraisal of the literature, nor has there been a review which has included literature pertaining to a paediatric population. The literature on paediatrics is of particular relevance given the fact that approximately 500,000 children

aged *younger than* 17 years are hospitalized each year with TBIs in the United States (Langlois & Thomas, 2005; Schneier, Sheilds, Hostetler, Xiang, & Smith, 2006). This statistic does not include those children with minor TBIs who were either seen by their family physician/paediatrician or remained undiagnosed. Furthermore, TBI is the leading cause of disability in those under the age of 24, and the peak age of occurrence for TBI is 15-24 years (Centre for Disease Control and Prevention, Division of Injury Response, 2006). Thus, the unique contributions of this paper are:

1. to systematically update and extend previous reviews on sleep and brain injury (Ouellet et al., 2004; Zeitzer et al., 2009) by conducting a thorough critical appraisal of the methodological quality of the literature that includes both children and adults and then, based on the identified strengths, weaknesses and inconsistencies, in the current literature;
2. to summarize the best evidence that currently exists with a goal of knowledge translating knowledge to clinical practice; and
3. to provide specific recommendations as to how the field can best be advanced in the most scientifically rigorous manner, given the unique complexities of this disorder.

In summary, the objectives of this paper are to systematically appraise the literature regarding sleep and wake disorders associated with TBI according to the following domains: epidemiology (including sports-related concussion), pathophysiology, neuropsychological implications, and intervention. Furthermore, we will identify practice points and provide recommendations for a research agenda, based on the current body of literature.

2.1.1 Definition of Sleep and its Functions

To fully grasp the significance of the impact of sleep disturbances post-injury, it is important to have a clear understanding of the actual definition of sleep and the critical roles and function it plays in human (and animal) physiology and homeostatic regulation. Tobler (1995) defined sleep as a physiological, complex, and integrated behaviour characterized by a significant reduction of the response to external stimuli, by a

characteristic posture usually in a special environment, by a characteristic change in the neurophysiological recordings of brain activity, and by a homeostatic increase after its restriction. Sleep is a critical function that serves to reverse, and/or restore biochemical and/or physiological processes that are progressively degraded during prior periods of wakefulness.

Sleep is believed to be essential for optimal immune function by influencing cellular (T-cell) immunity. Furthermore, an increase in growth hormone secretion is observed immediately following sleep onset, concurrently with a rise in cortisol in the latter half of sleep. This is critical for growth and development and is also important from the perspective of recovery from trauma, as not only does human growth hormone stimulate growth and cell reproduction, it also plays a critical role in cell regeneration. Furthermore, cortisol plays a crucial role in facilitating the body's adaptation to physical and mental stress, in the suppression of inflammation, enhancement of wound healing, modulation of plasma glucose, and increased production of erythrocytes (red blood cells) (Mullington, 2009).

Sleep is divided into non-REM (NREM) (rapid eye movement) and REM sleep. Studies of NREM and REM sleep and the importance of their temporal succession in both animals and humans reveal that these stages have been found to play key roles in certain types of memory and learning, as well as cerebral plasticity (Barkoukis & Avidan, 2007; Maquet et al., 2003; Walker, 2009). REM sleep, which occurs at the end of each sleep cycle, and the overall length of the REM cycle peaks prior to wakening also plays a key role in aspects of memory consolidation and new learning. Further, REM sleep during the neonatal period plays an important role in brain growth, neuronal maturation, connectivity and synaptic plasticity in infants (Mirmiran & Ariango, 2003). Thus, recognition of the critical role that sleep plays in endocrine and immune function, thermoregulation, cognition, and behaviour underscores the need to evaluate and optimize sleep during recovery from brain injury.

2.2 Methodology

An extensive and iterative literature search was conducted using the Ovid, Medline, PsychInfo, CINAHL, and EMBASE databases to ensure the capture of any relevant studies pertaining to the assessment of sleep after TBI. Medical subject heading terms included:

brain injuries or brain concussion or brain hemorrhage, traumatic or brain injury, chronic or diffuse axonal injury/sleep disorders/insomnia, and hypersomnia. The search was limited to articles published in English and from 1998-2009. Only peer reviewed full-text articles were considered for this study.

The search was initially exhaustive to include titles relating to both acquired brain injury and TBI, as the terms are sometimes used synonymously. This allowed us to ensure that we captured all relevant studies. Each article abstract was then reviewed to further ensure relevance. Additional search strategies were also employed and as such, the reference lists of all articles were scanned for additional studies, which may be relevant for review. Because the literature on the relationship between sleep disturbances and TBI is still developing, our inclusion criteria were quite broad, and all identified articles were reviewed.

We then subdivided the articles into five different domains of scientific inquiry, including epidemiology, pathophysiology, paediatrics, intervention, and neuropsychological implications. Because there are a limited number of articles in the different subcategories of focus, all identified articles from Level II to Level V, were included. In all, 68 articles were evaluated and 43 articles were included for purposes of this review. We excluded only those that we deemed to be opinion papers or consensus papers not based on the results of a specific scientific study.

To critically appraise and stratify the quality of the evidence, the articles were evaluated on their research design and scientific rigor. Although it was not our intention to conduct a meta-analysis such as those undertaken by the Cochrane Collaboration Group, the ranking criteria were selected from the literature on evidence-based practice in rehabilitation, with a goal of providing guidance to end users about studies likely to be most valid. Thus, the articles were categorized according to the scientifically validated hierarchy developed by Holm and edited by Boschen and colleagues (see Table 2) (Boschen, Gargaro, Gan, Gerber, & Brandys, 2007; Holm, 2000). Other rating systems are available (Downs & Black, 1998; Law, 2002; Sherrington, Herbert, Maher, & Moseley, 2000); however, the Holm hierarchy (Boschen et al., 2007; Holm, 2000) was chosen in order to better differentiate among the

published studies that exist at this point in the development of the literature on sleep and TBI. Given the early stage of development and the inherent complexities of the field, few randomized control trials (RCTs) have been conducted. It is, therefore, necessary to use a hierarchy that gives weight to non-RCT designs and also has a place for well-designed qualitative studies. Although the Holm hierarchy is an appropriate choice, it still did not fully differentiate the literature for our purposes Thus, the edited and published version used by Boschen et al. (2007) was used for this systematic review.

Table 2

Total Number of Articles Retrieved by Level of Evidence

Level of evidence	No. of articles	Article type
Level I[a]	0	Systematic reviews of randomized controlled trials (RCTs)
Level II	2	Properly designed individual RCTs of appropriate size
Level IIA[b]	2	Systematic reviews of case-controlled, cohort, or other experimental designs (including RCTs reviewed together with other experimental designs)
Level III	25	Well-designed trials without randomization, single group pre–post, cohort, time series, or matched case-controlled studies (also cross-sectional studies and case series)
Level IV	0	Well-designed non-experimental studies from more than one center or research group
Level IVA[b]	10	Well-designed individual nonexperimental studies, cost analysis studies, and case studies
Level V	5 + 1	Reports of expert committees, descriptive studies, clinical observations, opinions of respected authorities, testimonials
Total articles reviewed	42 + 3	

Note. [a] Holm (2000)
[b] Used the adaptation from Boschen et al. (2007) to further differentiate the evidence.

Boschen et al. (2007) added two additional levels to the Holm hierarchy: the first being Level IIA, which was added to evaluate review papers that did not meet the criteria for Level I as they included non-RCT designs, and, the second being Level IVA, which was added to separate out the well-designed nonexperimental research designs such as cost analyses, and qualitative designs from the purely opinion and descriptive studies classified as Level V articles.

To fully capture the literature in its current state of evolution, we also considered review articles of multiple well-designed studies (called Level I and Level IIA studies in this hierarchy) in our article inclusion criteria. These review articles were considered separately from the single-study articles, as they gave us a better perspective of the historical development of research in the field of sleep and TBI. Single studies were classified into levels based on the extent to which they met the criteria of the individual designated levels within this published hierarchy.

The process of assigning articles to levels was completed independently by two of the authors. Discrepancies were discussed and consensus was reached. Articles categorized as Level I or Level IIA were read and summarized but were not critically reviewed as they were review articles in of themselves. Published hierarchies do exist for the evaluation of systematic reviews; however as none of the review articles identified for this systematic review were systematic in nature, these hierarchies were not applicable.

Each of the articles was evaluated using a template generated for use in this study. The templates addressed the purpose, study design, sample, outcome measures, significant findings, relevant conclusions, and comments made by the authors of the articles, as well as any special notes from the article reviewers. Two of the authors and an undergraduate student completed the templates for the articles.

In order to critically appraise the quality of the articles, information was abstracted from the templates in regard to seven questions:

1. Were baseline characteristics described and equivalence of groups evaluated?
2. Was the intervention/methodology described in detail, that is, sufficient for replication?
3. Was blinding employed?
4. What was the sample size per group used for data analysis?
5. What was the attrition rate?
6. Were the outcome measures used for the study standardized?

7. Was there a follow-up data collection point?

This latter question was added specifically for the purposes of this review. The authors attempted to assess whether or not the intervention/methodology was described in sufficient detail to allow for understanding of the key elements and to allow for replication. These items were identified based on the items used in meta-analytic and other systematic reviews (Comper, Hutchison, Magrys, Mainwaring, & Richards, 2010). The presence of the above seven quality elements and their description in the articles was further rated on a three-point scale developed by Boschen et al. (2007) (see Table 3). The classification of the quality rating, the sum of the scores of each of the six elements, was made using a trichotomous scheme representing "Low" (summed score of <3), "Moderate" (summed score of ≥3 and <5), and "High" (summed score ≥5) quality determined by the developers, based on the previous work of Boschen and colleagues (2007). The abstraction and rating was performed independently by two of the authors and discrepancies were discussed and consensus reached.

Table 3

Criteria Used to Assess Quality of the Studies

Rating of assessed character-istic	Baseline character-istics: Described, equivalence	Blinding	Sample size (per group)	Attrition	Standard-ized outcomes	Descrip-tion of inter-vention	Length of follow-up
1	Both elements present in the article	Double	>75	<15%	All	Sufficient to replicate	> 3 months
0.5	Either characteristics described or equivalence noted but not both	Single	30-75	15-25%	Some	Some description	0-3 months
0	Neither presented	No blinding or not stated	<30	>25%	None	Not sufficient description	None

In addition, the articles on intervention were assigned a rating using the Downs and Black Rating System (Downs & Black, 1998). As the Downs and Black system is widely known

and accepted, we attempted to use this for the evaluation of all of the articles included. However, although it is an excellent tool for the assessment of the quality of evidence specific to intervention studies, we encountered a number of difficulties in applying it to the nonintervention studies reviewed in this article. Thus, the Downs and Black System was applied only to the intervention studies. The use of these two quality assessment methodologies for the intervention studies allowed for comparison and a more thorough description of the literature.

2.3 Results

2.3.1 Previous Reviews of Sleep

2.3.1.1 Disorders and Insomnia Following TBI: An Historical Overview of the Literature to Date

To date, three reviews of the literature pertaining to sleep and/or insomnia following TBI have been published (Orff et al., 2009; Ouellet et al., 2004; Zeitzer et al., 2009). The Ouellet thorough review (Ouellet et al., 2004), which we consider to be a Level IIA, was the first to be conducted on the topic of sleep disturbance following TBI. This review made a number of important contributions to our understanding of the early adult literature on this complex topic. The authors aimed to review the evidence on epidemiology, etiology and treatment of insomnia in the context of TBI, and to propose areas for future research.

With regards to the early literature on prevalence, Ouellet et al. (2006)reviewed nine studies and concluded that there were significant methodological issues in many of them, including lack of an operational definition of insomnia, and heterogenous approaches (lack of consistency) of the assessment measures used to evaluate the presence and clinical significance of the insomnia. Furthermore, they identified that most of the studies varied in terms of the time of evaluation post-injury, and the level of severity of the brain injury, making it difficult to draw any specific conclusions regarding prevalence.

Among the studies reviewed by Ouellet et al. (2006), they identified a range of reported symptoms of insomnia from 30-70% in patients with TBI, with symptoms of poor sleep

initiation and maintenance being the most prevalent. They also noted a range of time post-injury that symptoms (of insomnia) were present from 6-12 weeks post-injury up to several years. This was an important conclusion/observation as Ouellet et al. (2006) identified that "insomnia appears to develop a chronic course in a significant proportion of TBI patients" (Ouellet et al., 2006, p. 188).

In addition, they also identified a number of potential etiological factors that may be associated with the development of insomnia following TBI, including pre-disposing, precipitating, and perpetuating factors. Finally, they reviewed the literature on potential psychological and behavioural consequences of insomnia, and summarized the few studies on intervention, including pharmacotherapy and psychotherapies. The authors concluded the paper with some basic practical recommendations based on the literature to date. They felt comfortable concluding that insomnia is a common problem after TBI, the aetiology and maintenance of which is complicated. They further concluded that the presence of insomnia in patients with TBI likely has detrimental consequences; however more research is needed to identify effective treatments. They suggested that because insomnia can be chronic, combinations of pharmacological and psychological treatment options should possibly be used. Data collected from non-TBI patients suggest that cognitive behavioural therapy (CBT) has promise.

Orff et al. (2009) conducted an in-depth review of the literature, which we also identified as being Level IIA. This review, which builds on the previous work by Ouellet et al. (2004), included a clearly defined search strategy, key search terms and methodology. This review aimed to

> address the aetiology and implications of sleep problems in TBI, particularly mTBI, across 4 general domains of current scientific inquiry and observation: subjective impressions of poor sleep, objective changes in sleep-related parameters, alterations in circadian rhythms; and neurophysiologic and/or neuropsychologic abnormalities associated with TBI. (Orff et al., 2009, p. 155)

In the 5 years since the Ouellet et al. (2004) review, the prevalence of sleep disturbances following TBI (both subjectively reported and objectively measured, although the latter has some contrary findings) has been further established, and the literature has thus evolved to

more closely look at this complex disorder. With regards to subjective impressions of poor sleep, Orff et al. (2009) identified that the majority of studies surveyed had reasonably large sample sizes and provided replicable findings of insomnia in patients with TBI, particularly those with mild TBI (mTBI). Results of the studies surveyed on the topic of objective changes in sleep parameters were not quite so conclusive. The authors identified several studies with objective evidence of changes in sleep quantity and quality, as well as other sleep disorders such as obstructive sleep apnea (OSA), periodic limb movements (PLM) and narcolepsy. However, they also cite a number of studies where objective changes in sleep parameters were not found, despite subjective complaints of the patients. The authors cite similar methodological concerns as previously addressed by Ouellet et al. (2006), and further cite the lack of, or inconsistent reporting on, other important factors such as prior TBIs and past/current medical and psychiatric status, making it difficult to "evaluate the role of these variables in sleep-related outcomes, and complicating comparisons between studies" (Orff et al., 2009, p. 190).

Orff et al. (2009) reviewed the literature on TBI and circadian changes, and reported that although the literature is relatively sparse and somewhat conflicting at this time, there is a growing body of evidence to suggest that sleep disturbances following TBI may be due to alteration in the timing and rhythms of sleep (i.e., circadian rhythm sleep disorders) in a subset of patients. Additionally, they reviewed the literature on neurophysiologic and neuropsychological disturbances associated with sleep. They reported endocrine changes that may explain sleep disturbances in this population and also highlighted the limited but important research that suggests that deficits in cognitive performance after TBI may be related, in part, to the degree of sleep disturbance.

Consistent with the Ouellet et al. (2004) review, Orff et al. (2009) also summarized the literature on interventions to date, which remains limited to a few studies addressing pharmacotherapy and CBT. Finally, Orff et al. (2009) discussed limitations of the literature and identified that although the body of work has grown since the Ouellet et al. (2004) review, there remain similar methodological limitations such as small sample sizes, considerable variation in age, time since injury, level of severity and measures used to

assess sleep. Orff et al. (2009) recommend that future research needs to focus on uncovering the specific types, causes, and severity of TBI that most often lead to sleep problems; the consequences of sleep disturbance; and the most effective treatment strategies.

The final review studied for this paper is by Zeitzer et al. (2009). This review, which we identified as being a Level V and lacking the methodological strength of the previous two reviews, was conducted for the US Department of Veterans Affairs (VA). As such, its focus appears to consider insomnia in the context of TBI from the perspective of those assessing and treating veterans diagnosed with mTBI, hampered by a co-morbid sleep disorder. (Note: sleep apnea may in fact be pre-existing because it is, interestingly, present in about half of the Department of Veterans Affairs (VA) patient population (Zeitzer et al., 2009, p. 829). This review lacks a clearly defined objective and systemic review approach; however, the authors state that they will "consider insomnia directly caused by TBI (e.g., secondary to neural damage), indirectly caused by TBI (e.g., secondary to depression), and unrelated to TBI but occurring within individuals with TBI" (Zeitzer et al., 2009, p. 827).

Consistent with previous reviews, Zeitzer et al. (2009) cite studies of TBI populations of varying severities (mild-moderate) and varying lengths of time post-injury from 6 weeks to greater than 10 years. They reported that insomnia occurs in approximately 40% of individuals with a TBI of any severity, even though is more commonly reported among patients with mTBI, and is the most prevalent somatic complaint across all levels of severity. The authors also postulate two components of TBI-related insomnia including; First, that there is a general predisposition to develop sleep disturbance as a result of alterations or disruptions in neurotransmitters involved in the regulation of sleep (and they state further that the literature on this topic is for the most part limited to those with moderate-severe TBI). Secondly, there are often acute stressors which may trigger the insomnia. They highlight nonsleep comorbidities such as depression, pain and post-traumatic stress disorder, all of which are of particular relevance to individuals with TBI in general and to veterans with mTBIs. From this discussion, they highlight two future research questions. First, can mild TBI cause disruptions in the regulation of sleep? The

authors stated further that the literature on this topic is, for the most part, limited to those with moderate-severe TBI. Second, can acute stressors trigger the insomnia? They highlight nonsleep comorbidities such as depression, pain and post-traumatic stress disorder, all of which are of particular relevance to individuals with TBI in general and to veterans with mTBIs. From this discussion, they highlight two future research questions. First, can mTBI cause disruptions in the neurotransmitters critical for sleep and wakefulness? Second, what is the effect of psychiatric comorbidities on the occurrence or severity of insomnia in the context of TBI? The latter question aims to assist the physician in treating insomnia as a primary or secondary pathology.

Finally, the authors (Zeitzer et al., 2009) briefly summarize the literature on pharmacological and nonpharmacological treatments. As per the previous two reviews, the literature on treatment remains limited. As a result, these authors identify some cautionary caveats in the use of pharmacotherapy and describe nonpharmacological interventions such as CBT plus various combinations of sleep hygiene, sleep restriction and relaxation training. The authors highlighted the critical need for further nonpharmacological studies as viable alternatives to treatment of insomnia in mTBI. The authors conclude that more systematic research is required to "provide a foundation for an evidence-based medical approach to treatment of insomnia in the context of mTBI" (Zeitzer et al., 2009, p. 832)

2.3.2 Single Study Papers

As can be seen from Table 2 (p. 19), the majority of the literature (56%) is classified as Level III (Well-designed trials without randomization, single group pre–post, cohort, time series, or matched case-controlled studies [also cross-sectional studies and case series]). The next largest level is Level IVA with 24% of the categorized articles (well-designed individual nonexperimental studies, cost analysis studies, and case studies). The published literature is getting stronger as there are fewer Level V studies than Level III or IVA studies, but is still clearly under-developed as there are no Level I studies and few Level II or IIA studies.

Single study papers were organized into the following categories: Epidemiology (comparison group studies or single group/cohort studies), pathophysiology, paediatrics,

neuropsychology, and intervention (see Table 3 on p. 21, Table 4, Table 5, and Appendix A). It is important to note that there are Level III studies in each of the above categories but as of yet the Level II studies are only with regard to pharmacological interventions. Only one of the studies reviewed was considered of low quality, the majority were of moderate quality (89%), and only a few were of high quality (10%). Each of the studies is summarized in detail in Appendix A, which lists the level, quality, and key details relating to the conduction of the reported study. Each category of studies will be discussed below, in the order they appear in the table. Following each summary there will be an in-text box summarizing the research agenda and practice points identified with the authors of the reviewed studies, followed by our recommendations.

Table 4

Article Scope and Level of Articles

Article scope	Total no. of articles	Level II/IIA	Level III	Level IVA	Level V
Epidemiology – Comparison group	9		9		
Epidemiology – Single group/cohort	14		5	6	3
Pathophysiology	3		2	1	
Paediatrics	6		6		
Neuropsychology	4		1	2	1
Intervention	6	2	3	1	
Reviews	3	2			1
Total	45	2/2	26	10	5

Table 5

Article Purpose and Quality of Article

Article scope	Total	Moderate quality				High quality	
		3	3.5	4	4.5	5	6.5
Epidemiology – Comparison group	9			6	3		
Epidemiology – Single group/cohort	14	1	3	4	4	2	
Pathophysiology	3		1	1	1		
Paediatrics	6 [a]		2	1	1	1	
Neuropsychology	4		1	2	1		
Intervention	6		1	1	2	1	1
Reviews	3						
Totals	45	1	8	15	12	3	1

Note. [a] One article was of low quality with a rating of 2.5.

2.3.2.1 Epidemiology

The evidence relating to the epidemiology of sleep and wake disturbances following TBI has historically been the primary focus of the literature, comprising 23 of the 43 papers across the five subtopics we identified for this review. Epidemiological investigation of a phenomenon is a necessary starting point as it provides a solid foundation for all further investigations to follow. We subdivided the studies on epidemiology, all of which were rated at Level III study designs, to include nine papers with a comparison group, all of moderate quality, and 12 articles that used a single group design, 10 of which were moderate quality, and two were of high quality (Baumann, Werth, Stocker, Ludwig, & Bassetti, 2007; Castriotta et al., 2007). Both of these studies were also classified as Level III. Amongst the single group studies, there were five rated as Level III, five rated as Level IVA, and two rated as Level V. The use of a comparison group is a stronger design, however our quality rating scheme studies included several elements, weighted equally, to assess overall quality so that a study weak in one area can be strong in other areas.

There are several important elements that should be addressed in a good quality epidemiological study. Recruitment is a key issue and recruitment methods must be

carefully considered to make sure that any selection bias is eliminated. Recruitment from the perspective of time post-injury is also a factor for consideration in that it allows us to observe the developmental time course of the disorder. Amongst the papers we reviewed, 65% of the studies (15/23) used consecutive recruitment; however, only 13% (3/23) used consecutive recruitment directly from the acute setting. Twenty-six percent were consecutively recruited as patients entered rehabilitation and the remaining 26% were recruited while in rehabilitation or upon discharge from rehabilitation. Parcell, Ponsford, Redman, and Rajaratnan (2008) recruited all patients with TBI, with no preference for those with sleep complaints, thus reducing bias in their sample. The remainder of the studies included retrospective chart review or recruitment by advertising. In contrast to the Parcell et al. (2008) study, the study by Ouellet et al. (2006), with the largest sample size of 452, recruited participants with reported symptoms of insomnia via mailings sent to 1,500 prospective participants from archives of Québec City's largest rehabilitation centre, local brain injury associations and support groups. The authors specifically reported using liberal inclusion criteria to try and capture a "broad portrait of the TBI population" (Ouellet et al., 2006, p. 201).

It is also important to consider possible confounders or variables that influence interpretation of the findings, such as pre-existing, concurrent and secondary co-morbidities; age at onset of injury; time since injury; severity of injury; etiology of injury; and gender. In an "ideal" study the sample population would be large enough to allow stratification on some or all of these variables, so that the findings would be more generalizable and create a more thorough picture of the phenomenon.

Overall, the objectives of the epidemiological studies reviewed for this article were to document the incidence, prevalence and nature of sleep disturbances post-TBI, primarily "insomnia" per se, with the inclusion of the most recent data relating specifically to sports-related concussion. It has been consistently reported in the literature that individuals with TBI experience symptoms of insomnia and other sleep disturbances across the spectrum of recovery from the acute stage and beyond, across all levels of severity, with some continuing to report sleep disturbances for many years post-injury (Beetar et al., 1996;

Burke et al., 2004; Castriotta & Lai, 2001; Fichtenberg et al., 2002; Ouellet et al., 2004, 2006; Parcell et al., 2006; Rao et al., 2008; Schreiber et al., 2008; Verma et al., 2007; Williams et al., 2008).

Thus, in order to try and present the literature in a manner which might further elucidate our understanding of the developmental course of post-traumatic sleep disturbances over time, we attempted to discuss the studies from the perspectives of sleep in the acute stage, early recovery/rehabilitation (to 1 year), 1-3 years and beyond. However, consistent with the reports of Ouellet et al. (2004) and Orff et al. (2009) in their previous reviews, we experienced difficulties in doing so, particularly for those studies (the majority of which we identified) that were cross sectional, i.e., evaluating sleep at only 1 time period.

Most studies clearly identified the average time post-injury of their participants and the range/standard deviation, but the ranges were in fact, quite wide. Amongst the studies which utilized a comparison group, (i.e., those studies which were methodologically stronger than those studies that did not involve a comparison group), the ranges of time post-injury were (in chronological order from publication date): from 2.7 months – 5 years, average 2 years post (Beetar et al., 1996); 2 weeks-53 months average, 3.8 months post (Fichtenberg et al., 2002); 7-41 months, average 20.96 months post (Ouellet et al., 2006); 20-1194 days, average 230 days (Parcell et al., 2006); 12 mos-21 years, mean not given (Schreiber et al., 2008); 74–1194 days, average 516 days (Parcell et al., 2008); 12.3–43.3 months, average 27.8 mos (Williams et al., 2008); up to 1-year post, specifics not given (Gosselin et al., 2009). Thus, over-all amongst these studies, we identified a 21-year range in time post-injury among participants. The results however, were not stratified in any of the studies by time post-injury, thus making it extremely difficult to draw any definitive conclusions regarding the developmental time course of the sleep disorders.

Further, sleep disorders may well be confounded over time by the subsequent development of depression, anxiety, reduced activity and weight gain, etc., again making it difficult to draw specific conclusions about the aetiology of these disorders. It is necessary to acknowledge and mitigate potential confounding factors on the results, whether these are factors that were pre-existing to the brain injury or have developed secondary to the

brain injury. However, from the perspective of recruitment at various times post-injury, there were studies which reported on sleep findings including both prevalence and nature, at specific time points across different levels of severity. Thus we have attempted to summarize the literature regarding the prevalence and nature of sleep disorders post-TBI based on the source of patient recruitment: acute/post-acute, rehabilitation and community. Only those studies which delineated recruitment by time post-injury and level of severity, as well as stratifying results according to source of patients (e.g., acute care, rehabilitation settings) and level of severity are included below (thus those studies which did not stratify their findings by level of severity are NOT included). In addition, we only included studies that had substantial measures of sleep versus a single item documenting sleep problems.

2.3.2.1.1 Patients recruited from acute and post-acute care

We identified five studies which recruited participants from acute care settings (Fichtenberg et al., 2002; Makley et al., 2008; Parcell et al., 2008; Rao et al., 2008; Watson, Dikmen, Machamer, Doherty, & Temkin, 2007).

*Acute mild***.** Chaput, Giguere, Chauny, Denis, and Lavigne (2009) conducted a retrospective chart review to determine the prevalence of sleep complaints in a sample of 443 patients diagnosed with mTBI, at two time points: 10 days and 6 weeks post-injury. Of this sample, 13.3% of those reported sleep changes at 10 days post-injury, and this increased to 33.5% at 6 weeks post-injury with a smaller sample. Further, the prevalence of sleep complaints at 6 weeks was 2.9 times more likely if such a symptom was present at 10 days ($p = 0.004$), and associated with concomitant headaches, depressive symptoms and irritability. Given the large sample size and the fact that they recruited all of those within the diagnostic category rather than just those with sleep complaints, the sample bias is minimized and the results are more generalizeable to the whole mTBI population. The nature of the sleep complaints, however, was not delineated.

*Acute and post-acute moderate-severe***.** Makley et al. (2008) followed a sample of 14 patients with moderate-severe injuries recruited at 9 to 23 days post-injury from acute care, and reported that 78% had severely impaired mean sleep efficiency (< 63%) as measured by

actigraphy These patients were subdivided into 2 groups, those with ongoing post-traumatic amnesia (PTA), and those whose PTA had resolved. Of significance, they reported that sleep efficiency improved once patients were no longer in PTA, ($p = 0.032$). Baumann et al. (2007) consecutively recruited 96 patients within the first 4 days after TBI and at 6 months post, 65 patients were evaluated, using a combination of polysomnography (PSG), Multiple Sleep Latency test (MSLT), actigraphy and clinical interview. They determined that at 6 months post-injury, among patients across all levels of severity (60% moderate-severe), 72% had sleep problems, 28% had subjective daytime sleepiness, 25% had objectively measured daytime sleepiness, 17% reported fatigue and 22% reported *"sensu strictu"* (an increased sleep need over 24hours). A further 5% had insomnia. The authors further noted that in 43% of patients, the only possible cause of these problems was directly attributed to the TBI.

Rao et al. (2008) recruited a sample of 54 within 3 months of trauma across all levels of severity; however all had experienced a loss of consciousness. Results of the Medical Outcome Scales for sleep indicated significantly increased sleep disturbance ($p = 0.018$), decreased sleep adequacy ($p = 0.023$) and increased daytime sleepiness ($p = 0.0002$) in comparison to self-reports of pre-injury sleep. Watson et al. (2007) looked specifically at the prevalence of hypersomnia in a consecutive sample of 346 patients with TBI recruited from admissions to a Level 1 trauma hospital, in comparison to trauma controls (without TBI) and trauma-free controls. Data on sleepiness was collected at 1 month post-injury, with follow-up at 1 year. Level of severity was determined by time to follow commands according to the motor component of the Glasgow Coma Scale (GCS) (Teasdale & Jennett, 1974). Although 78% of participants took less than 24 hours to follow commands, they presented with serious enough symptoms in the emergency room that they were admitted to hospital and as such we have included them in discussion with moderate-severe. At 1 month post-injury, 55% of all participants with TBI endorsed one or more sleepiness items on the Sickness Impact Profile, in comparison to 41% of trauma controls and 3% of trauma free controls ($p < .001$).

2.3.2.1.2 Patients recruited from rehabilitation populations

Mild. We identified only four recent studies which recruited mild persons from a rehabilitation outpatient population. Beetar et al. (1996) conducted a retrospective chart review to determine the prevalence of sleep complaints in a consecutive series of 202 patients with TBI referred for neuropsychological assessment. The sample included 127 mTBI patients, 75 moderate-severe and 123 non-TBI controls). The authors found that overall, 56.4% of the TBI patients had significantly more complaints of insomnia in comparison to controls (30.9%), ($p < 0.001$), and the mTBI group reported approximately 50% more insomnia complaints than those with moderate-severe injuries ($p < .001$). This study was an important early contribution to the literature on sleep and TBI. Even though they did not use an operational definition of insomnia, their large sample size, use of a control group and delineation of results by severity provided a strong foundation for future research. With regards to prevalence**,** Clinchot, Bogner, Mysiw, Fugate, and Corrigan (1998) also reported on a sample of patients recruited from consecutive admissions to rehabilitation and contacted at 1 year post-injury. Clinchot et al. (1998) found that approximately 75% (as indicated by bar graph, see Figure 1) of individuals (GCS 13-15) subjectively reported sleep disturbance.

Schreiber et al. (2008) looked at the nature of sleep disturbance, conducting a retrospective study of 26 patients with mTBI and sleep disturbance who were consecutively admitted to ambulatory rehabilitation. In comparison to healthy age and sex-matched controls (who had routine sleep evaluations as part of a pre-employment assessment procedure), the mTBI group had objective changes in sleep architecture, including increased light sleep (nREM) in 54.5% of participants in comparison to controls (46.6%), and significantly lower total sleep time ($p < 0.05$). They also reported increased excessive daytime sleepiness (EDS) objectively measured by MSLT in comparison to controls (higher number of falling asleep episodes ($p \leq 0.05$) and shorter time to fall asleep ($p < 0.0005$). Baumann et al. (2007) (also discussed in Acute-post-acute moderate-severe) reported objectively measured sleep efficiency of 92% amongst their participants with mild TBI; however, they identified 2 participants (13%) with sleep efficiency well below age adjusted 25% percentile values. It is important to consider that the findings of these three studies may

not be generalized to the population of mTBI as a whole as despite the fact that the participants are classified as mild, they all required rehabilitation and or were referred for neuropsychological evaluation, thus placing them in a more "involved or 'severe/complicated" category of "mild".

Moderate-severe. Despite the fact that we identified seven studies which looked at the prevalence and or nature of sleep disturbances in samples recruited from a moderate-severe rehabilitation population (Castriotta et al., 2007; Fichtenberg, Millis, Mann, Zafonte, & Millard, 2000; Fichtenberg et al., 2002; Masel, Scheibel, Kimbark, & Kuna, 2001; Verma et al., 2007; Worthington & Melia, 2006), only the most recent (and higher quality study) stratified or reported results according to severity (Castriotta et al., 2007), with the exception of the earlier work by Clinchot (1998). Clinchot et al. (1998) (recruitment described above) found that approximately 57% of patients with GCS 8-12, 24% of patients with GCS 5-7, and 40% of patient with GCS 3-4, reported subjective sleep complaints. Castriotta et al. (2007) conducted an objective evaluation of sleep in 87 patients who were at least 3 months post-injury, recruited from the rehabilitation services at three academic medical centres. Abnormal sleep studies were found in 46% of participants. With regards to the nature of the sleep disturbances, 20% had Obstructive Sleep Apnea (OSA), 11% had post-traumatic hypersomnia, 6% had narcolepsy and 7% had Periodic Leg Movements (PLM). Among all participants 22% had objective excessive daytime sleepiness as measured by MSLT (Multiple Sleep Latency Test). Of interest, they identified no differences in injury severity and or time post-injury between sleepy and nonsleepy participants with TBI.

Finally, we identified two studies that recruited patients from rehabilitation and although they identified objectively measured sleep and wake disturbances among participants, neither study identified any significant differences in injury severity or time post-injury between sleepy and nonsleepy participants. Castriotta et al. (2007) examined the prevalence of sleep disorders in a prospective sample of 87 patients with TBI recruited from the rehabilitation services at three academic medical centres. Abnormal sleep studies (PSGs) were found in 46% of participants, including 23% with OSA, 11% with post-

traumatic hypersomnia, and 7% with PLMs. Objective excessive daytime sleepiness was found in 25% of participants. Consistent with the findings of Verma et al. (2007), OSA was more common in obese participants (body mass index (BMI) $\geq$ 30). Further, these investigators did not find any differences in severity of injury or time post-injury between sleepy and nonsleepy participants ($p < 0.05$).

2.3.2.1.3 Patients recruited from the community

We identified eight papers which recruited samples of individuals with TBI who had returned to the community (Clinchot et al., 1998; Ouellet et al., 2006; Parcell et al., 2006; Parcell et al., 2008; Schreiber et al., 2008; Verma et al., 2007; Watson et al., 2007; Williams et al., 2008).

Mild. Williams et al. (2008) studied the extent and nature of sleep complaints in a sample of nine university students with previous mTBIs (with a range of 1.4-3.6 years post-injury) in comparison to age and gender matched controls. They identified 4% less efficient sleep, shorter REM onset latencies and longer sleep onset latencies in comparison to controls, objectively measured by PSG. While this study is quite thorough and rigorous in design, the small sample size and "sample of convenience" (i.e., student volunteers), weakens the generalizability of the findings. Schreiber et al. (2007) characterized the nature of sleep disturbances in a sample of 26 chronic mTBI patients with sleep complaints, at least 1 year post-injury. They reported changes in sleep architecture (as measured by PSG) including increased light non-REM sleep, in 54.5 %($\pm$13.4) in comparison to controls (46.6 $\pm$10.4%).

Moderate-severe. Parcell et al. (2006) reported on a sample of 63 participants with TBI consecutively recruited after discharge from rehabilitation, in comparison to 63 age and sex matched controls. Eighty percent of patients reported subjective changes in sleep relative to controls (23%), including more night-time awakenings, and longer sleep onset latency. In another study, Parcell et al. (2008) recruited 10 community based participants with TBI and 10 age- and sex- matched and reported objectively measured increases in slow-wave sleep, reductions in REM sleep, and reduced sleep efficiency in comparison to controls, as well as subjective reports of poorer sleep quality.

Ouellet et al. (2006) recruited a sample of 452 participants from mailings distributed to 1500 people with TBIs identified through the archives of the rehabilitation centre, as well as TBI associations and support groups. Their sample included 59.9% with severe injuries, 23.3% with moderate, 13.7 with mild and 3.1 with 'minor' TBIs. Participants completed a detailed questionnaire, which was then mailed back to the authors, who identified that 50.2% of their sample reported insomnia symptoms, and 29.4% fulfilled the diagnostic criteria for an insomnia syndrome. This study continues to have the largest sample size of all of the literature to date pertaining to the prevalence of insomnia following TBI. In addition, it is one of the few that actually delineated between those who present with symptoms of insomnia and those who meet the diagnostic criteria for insomnia, thus providing a more reliable and valid estimate of the true prevalence. It is not possible, however, to completely eliminate sample bias without having information regarding the 1000 others who chose not to participate.

In another study, Ouellet and Morin (2006) examined the nature of insomnia in the context of TBI by recruiting a sample of 14 adults with TBI who presented with an insomnia syndrome (9 of whom were moderate-severe), and 14 healthy age and sex matched controls. It was not clear from the paper how or where the participants were recruited. The authors reported that 71% of participants had objective findings of insomnia including more awakenings and shorter REM onset latencies. Further, in comparison to controls, those with TBI had significantly more awakenings longer than 5 minutes ($p = 0.059$) as well as significantly shorter REM latency (for those with TBI taking no medications) ($p = 0.050$). In the 1 year follow-up to their study of the prevalence of hypersomnia in the acute stage post-TBI, Watson et al. (2007) found that 27% of participants continued to endorse subjective symptoms of sleepiness, in comparison to 23% of trauma controls and 1% of nontrauma controls ($p< 0.001$). However sleepiness did improve in 84-100% of participants with TBI, with the smallest improvement (84% being in the mildest group, $\leq$ 24 hours to respond to commands). Verma et al. (2007) objectively examined the nature and spectrum of sleep disorders in chronic TBI by recruiting a sample of 60 patients who presented with post-injury sleep complaints. It is not clear where or how the participants were recruited. Sixty percent of the sample had moderate-severe injuries. Hypersomnia

was the presenting complaint in 50% of all participants that the authors reported was "mostly due to" underlying sleep apnea, narcolepsy and PLMs. Of interest, 45% of the sample exceeded a BMI of 30, which is considered to be obese. Insomnia was the presenting complaint in 25% of participants, and half of those had difficulties with sleep onset.

Sport-related concussion. New to the literature in 2009 is a study which evaluates sleep following sport-related concussions. Gosselin et al. (2009) examined both subjective and objective sleep quality in 10 participants/athletes with sport-related concussion, and compared their findings to those of 11 nonconcussed control athletes from noncontact sports. The concussed group had a history of, on average, 4.6 (±2.1) concussions, sustaining at least one in the previous year. Objective measures of sleep included two consecutive nights of PSG, EEG spectral power, and subjective measures of sleep included the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Post Concussion Symptom Scale, as well as a subjective questionnaire, developed specifically for the study. The authors reported that although the concussed athletes identified more symptoms and worse sleep quality than controls; this was not corroborated by any polysomnographic variables, or on REM and nREM sleep quantitative EEG variables. However, concussed athletes did show considerably more relative delta activity and reduced alpha activity and relative alpha power during wakefulness than controls. Based on these findings, they concluded that sport-related concussions are thus associated with wakefulness problems, rather than sleep disturbances *per se*. While this study has a small sample size and as such their findings are preliminary, their strong methodological design is such that this is an important first step in examining this population. Their findings are relevant and timely, given that sports related concussions occur at a predictable rate in "high risk" sports (i.e., football, hockey, etc.) ranging from 7-12% of its population in any given year, and the sequelae of sport-related concussion is currently receiving much attention (Covassin, Swanik, & Sachs, 2003; Covassin et al., 2006; Dvorak, McCrory, & Kirkendall, 2007).

2.3.2.1.4 Prevalence

As the literature has continued to evolve, we attempted (as have others before us) to identify ranges of the prevalence of sleep disturbances identified amongst the studies based on time post-injury of recruitment. The results of these studies confirm that disorders of sleep and wakefulness are prevalent across all stages of recovery from TBI from the early acute stage until many years post-injury, across all levels of severity. However, defining conclusive "ranges" continues to be problematic due to the heterogeneity within and between samples, inconsistencies in the measures used, different study objectives and variations in reporting. Some studies utilized percentages for reporting findings, others reported on regression analysis of sleep along with various associated phenomenon (i.e., depression, anxiety), others identified changes in sleep architecture, some looked specifically at insomnia as a global phenomenon, while others reported on the symptoms of insomnia and some looked at other types of sleep disorders such as hypersomnia in of itself, or secondary to apnea, etc. As such, a valid synthesis of prevalence rates among studies remains elusive, and larger epidemiological studies across levels of severity and varying time points are warranted.

2.3.2.1.5 Methodological limitations

Further, while the studies continue to become more scientifically rigorous as the literature evolves, the results to date are representative of methodological limitations in study design, as most of the literature is based on a clinical subset of TBI survivors who (a) present with sleep complaints, therefore introducing bias into the sample, and (b) have received rehabilitation and therefore, represent a subset of this patient population with likely more severe injuries, even those who are classified as 'mild'. Thus it is likely that the data are skewed and are not fully representative of the TBI population as a whole. However, Parcell et al. (2008) specifically identified that their sample of 10 included 'the first 10 willing participants, with no preference for patients with sleep complaints' and Fichtenberg et al. (2002) recruited a prospective sample of 50 consecutive admissions to an outpatient rehabilitation program. The advantage of recruiting consecutively upon admission to the acute setting or from the emergency room is that all patients diagnosed

with TBI are included in the study sample regardless of whether they require post-acute care, or not. By following patients from the acute stage the issue of time since injury becomes negated as all of the sample will be entered into the study at time of injury. As soon as recruitment takes place after the acute stage, researchers are already introducing forms of selection bias into the sample that should be addressed when discussing the generalizability of the findings. Given that such a small percentage of the studies were able to recruit consecutively from the acute setting the epidemiological understanding of this phenomenon is going to be fraught with issues of generalizability and difficulty in making clear conclusions.

An ideal study would follow a large sample consecutive series of patients from acute care for at least 3 years to understand how sleep problems manifest themselves, or not, and how these change over time, considering natural recovery by levels of severity.

Confounds. Some of the studies made sure to exclude concurrent potential confounders while other collected data on potential confounders (usage of caffeine, alcohol, medications, or drugs, BMI, and emotional state). However, with the exception of emotional state, (which is also identified as a con-current risk factor) the results were not stratified according to any of these confounds, nor were they addressed in discussion. Thus we are only able to comment that these confounders exist, but are not able to make any definitive comments regarding their influence.

*Risk factors***.** Ten studies identified risk factors specifically associated with insomnia post-TBI, and two studies identified risk factors for other types of post-traumatic sleep and wake disorders. Beetar et al. (1996) identified pain and mTBI as being risk factors for insomnia complaints in a case controlled sample of 200 TBI patients of mixed severity. Among a sample of 91 consecutive patients admitted to an outpatient rehabilitation program, Fichtenberg et al. (2000) identified three risk factors associated with insomnia including milder injuries, the presence of pain, disturbance of sleep and depression. Of the three factors, depression had the strongest association with insomnia. Consistent with Fichtenberg et al.'s (2000) findings, Ouellet et al. (2006) reported that among a sample of 460 survivors recruited from the community (averaging 7.85 years post-injury, 83.2% of

whom with moderate-severe injuries), risk factors for insomnia included milder injuries, depression and pain. They also identified high levels of fatigue as a further risk factor.

Among a sample of 60 patients with varying levels of severity, ranging from 3 months-2 years post-injury, Verma et al. (2007) noted that those with complaints of insomnia had elevated Beck Depression Inventory (BDI) scores and Hamilton Anxiety (HAS) scores, thus further confirming that depression and anxiety are risk factors for insomnia post-TBI across all levels of severity. They also identified 45% of their sample as having a significantly high BMI. Chaput et al. (2009) identified headaches, depressive symptoms and irritability as co-occurring with sleep complaints in a sample of 443 patients with mTBI, at both 10 days and 6 weeks. Rao et al. (2008) also identified depression and anxiety as co-existing risk factors for symptoms of insomnia. Clinchot et al. (1998) was the only study to identify gender (female) as being a risk factor for symptoms of insomnia ($p = 0.033$), in addition to older age ($p = 0.035$), milder injuries, and GCS greater than 7 ($p = 0.034$). Baumann et al. (2007) identified that severe TBI was associated with the development of post-traumatic hypersomnia ($p = 0.02$), but not with the presence, characteristics and severity of other post-traumatic sleep disorders. The association between more severe TBIs and the development of hypersomnia was also confirmed by Watson et al. (2007). Castriotta et al. (2007) identified that among the 46% of their sample with abnormal sleep studies (with five different types of sleep and or wake disorders), the sample was significantly older than the non-sleep disordered participants ($p < .01$) and had a significantly higher BMI ($p < .05$).

Sample size. Traumatic brain injury is very heterogeneous and as a result it is complicated to conduct research that is generalizable. Ideally studies would be able to recruit a large number of patients so that stratification on a number of variables would be possible: age-at-injury, gender, aetiology of injury, severity of injury, and time since injury. It is necessary to refine the study question so that it is clear what is being studied and also so that one study is not expected to do more than is reasonable. When the study question is too broadly defined and the sample size small and heterogeneous, it is difficult to make conclusions that will advance the understanding of this phenomenon. Only 39% (9/23) of

the studies reviewed used sample sizes of greater than 75. Thirty-five percent of the (8/23) studies involved studies with sample sizes of less than 30 and thus were compromised in their statistical analysis and their ability to generalize to the different subgroups of brain injury.

Definition of insomnia. Another methodological limitation, also identified by Ouellet and Morin (2006) is the lack of an operational definition of insomnia. Among the 5 comparison group studies which evaluated subjective reports of insomnia, sleep and hypersommnia post-injury (Beetar et al., 1996; Fichtenberg et al., 2002; Ouellet & Morin, 2006; Parcell et al., 2006; Watson et al., 2007) only two utilized an operational definition of insomnia, the International Classification of Sleep Disorders and the DSM-IV (Fichtenberg et al., 2002; Ouellet & Morin, 2006). Related to this is the lack of consistency in or development of an operational framework for assessing severity of brain injury. Many studies use the Glasgow Coma Score (GCS) to assess severity but the GCS is not always available and other factors are included: length of PTA, period of loss of consciousness (LOC) cerebral computed tomography (CT) findings, and neuropsychological findings. One study (Watson et al., 2007) determined injury severity based on time to follow commands. Baumann et al. (2007), one of the two methodologically strongest studies reviewed, specifically cited using GCS and CT findings based on Marshall et al.'s (1992) criteria (I=no visible intracranial pathology, II-IV=midline shift, and V=mass lesion). It is necessary that there be consistency as to how to combine all of these factors together so that severity distinctions can be enabled when only some of the above features are present.

*Measures***.** As per the comments of Orff et al. (2009) there is also a significant discrepancy amongst the measures utilized. Among the 23 studies we evaluated under the category of epidemiology, investigators used 19 different methods to evaluate sleep, of which 4 are objective (PSG, actigraphy, MSLT, Multiple Wake Test (MWT)). There is no gold standard of standardized instruments that is accepted. While locally developed measures and those that are clinically developed may be very useful it is impossible to compare from one study to the next when different types of measures are being used to assess the outcomes. The issue is that sleep itself is very difficult to assess, as it is comprised of many components. It

would seem that among the validated instruments the most commonly used and accepted are the Diagnostic Interview for Insomnia (DII), Insomnia Severity Index (ISI), PSQI, and the ESS. It has been proposed that the MWT may be more suitable for this population than the MSLT, as daytime sleepiness seems to be a hallmark of this condition. One study (Rao et al., 2008) utilized the 12-item Medical Outcome Scale for Sleep (Hayes, Martin, Sesti, & Spritzer, 2005), which has been found to have good psychometric properties and has been found to be useful to assess sleep problems in adults. Each of these instruments contributes a unique component to the assessment of insomnia and sleep difficulties and as such should be used in combination, rather than in isolation.

The subjective or self-report measures ranged from the early work of Beetar et al. (1996) which relied on a chart review, concluding that 'a sleep problem was judged as present if it mentioned in the chart as reported by the patient' (Beetar et al., 1996, p. 1299) to the more robust PSQI used by Fichtenberg et al. (2002) (and validated for use with TBI patients), the battery used by Ouellet et al. (2006) which included the DII, ISI, Multidimensional Fatigue Inventory, in addition to other measures and nocturnal PSG, the sleep diaries and ESS used by Parcell and colleagues (2006, 2008). The most commonly used measures included the PSQI, PSG, and some form of sleep diary. It is positive to note that as the literature evolves, over-all, the use of measures to evaluate sleep and wake disorders has become increasingly comprehensive, sensitive and 'robust' over time. This in and of itself, however, further emphasizes the weakness of recent studies that rely on limited and or weak measures, such as study by Watson et al. (2007). While we recognize that this study was part of a larger study, and had the strength of a follow-up in its design, their sole reliance on data obtained via 4 questions about sleep from the Sickness Impact Profile weakens the validity/generalizability of their over-all findings.

Table 6

Practice Points and Proposed Research Agenda: Epidemiology

Practice points	Research agenda
1. Sleep and wake disorders are present across all levels of severity at all stages across the continuum of recovery following TBI. 2. Sleep and wakefulness should be routinely and systematically assessed for the duration of medical and neuropsychological follow-up after TBI. 3. Risk factors for insomnia include mTBI, pain, anxiety, depression, fatigue, and older age. 4. Risk factors for hypersomnia include more severe TBIs. 5. Increased BMI (> 30) is a risk factor for OSA. 6. The PSQI, followed by the ISI are appropriate measures for initial screening and corroboration of the impact of the problem.	1. A large scale multi-centre collaborative trial involving all those with TBI (i.e., not limited to those who present with sleep problems) recruited in the acute stage and followed longitudinally into the community and evaluated at regular time points is warranted. 2. Functional measures should be used in additional to formal measures of cognition.

2.3.2.2 Pathophysiology

We identified three papers all of moderate quality which look at varying aspects of pathophysiology of sleep/wake disturbances post-TBI, including two Level III studies (Ayalon, Borodkin, Dishon, Kanety, & Dagan, 2007; Baumann et al., 2005) and one Level IVA study (Quinto, Gellido, Chokroverty, & Masdeu, 2000). In 2005, Baumann et al. sought to test the hypothesis that deficiencies in hypocretin-orexin-1 neurotransmission in acute TBI may play a role in the emergence of subsequent sleep/wake disorders. Hypocretin-orexin 1 (Orexin A) is an excitatory hypothalamic neuropeptide involved in the regulation of the sleep/wake cycle, and its levels are typically reduced in persons with narcolepsy. Hypocretin-1 levels were measured in 44 patients by radioimmunoassay, at 1-4 days post-TBI (Males = 32, 31 patients severe TBI, 8 modTBI and 5 mTBI), and compared to

hypocretin-1 levels in healthy controls (n = 20). Their results indicated that in comparison to controls, hypocretin-1 levels were abnormally lower in 95% of patients, with moderate-severe TBI, and in 95% of patients with post-traumatic brain CT findings. The authors postulate that hypocretin-1 deficiency following TBI may be reflective of hypothalamic damage (specifically to the posterolateral hypothalamus) and may be linked with the frequent development of post-traumatic sleep wake disorders. These findings are an important contribution to the determination of risk factors.

Ayalon et al. (2007) conducted a study to diagnose and describe the physical and behavioural characteristics of circadian rhythm sleep disorders (CRSDs) in patients with mTBI. Forty-two patients with mTBI and complaints of insomnia were screened, and those who were suspected of having CRSD underwent further diagnostic evaluation. In total 15 of the 42 patients (36%) were formally diagnosed with CRSDs, eight patients displayed a delayed sleep phase syndrome (DSPS) and seven patients displayed an irregular sleep-wake pattern (ISWP). All patients exhibited a 24-hour period of melatonin rhythm and those with DSPS exhibited a 24-hour periodicity oral-temperature rhythm, however, 3/7 with ISWP lacked such a daily rhythm. Further, the patients with ISWP exhibited smaller amplitudes of temperature rhythm. Given that the authors found that as many as 36% of their particular sample had been diagnosed with insomnia, when in fact they had a CRSD, they conclude that CRSD may be a relatively frequent sleep disorder among these patients, and that misdiagnosis of patients with CSRD as insomniacs may lead to inappropriate prescription of hypnotic medications.

Quinto et al. (2000) described the case of post-traumatic DSPS in a 48-year-old male 4 years post-TBI (note: the authors use the term cerebral concussion, however as the patient was in coma for “several days”, we will consider this to be a severe TBI (sTBI)). While the patient was 4 years post-injury, the emergence of his sleep onset insomnia was during the acute phase of recovery. Since his injury, it took him 1 to 2 hours to fall asleep. He reported through a sleep diary that he would go to bed between 3:00 and 5:00 a.m. and awaken after 1 to 1 1/2 hours, return to sleep and awaken between 11:00 a.m. and12:00 p.m. These findings were confirmed by actigraphy. The patient did not have any other medical or

psychiatric disorders. Circadian rhythms are quite strict and are in fact slightly less than 24 hours in humans. The "circadian clock" located in the superchiasmatic nucleus (SCN) of the hypothalamus, serves to keep physiologic functions in synchrony with each other and with the environmental light/dark cycle, thus making a small daily phase advance to entrain to the 24-hour day. A decreased ability to make this phase advance in response to environmental cues is thought to be the underlying pathophysiology behind DSPS, and the authors of this study postulate that damage to the SCN sustained during trauma may result in circadian cycle disorder.

Table 7

Practice Points and Proposed Research Agenda: Pathophysiology

Practice points	Research agenda
1. It may be of benefit to measure hypocretin-1 in patients with moderate-severe TBI (who are being monitored for ICP) during the acute stage, as a potential marker/risk factor for the emergence of sleep and wake disorders 2. Lesions/damage to the hypothalamus are a risk factor for sleep/wake disorders following TBI 3. Awareness of delayed sleep phase syndrome (DSPS) as a possible consequence of TBI is important as its symptoms may be overlooked and attributed to the 'typical' post-concussion syndrome complex	1. "Future research specifically designed to explore the role of neurophysiologic and psychological factors in the emergence of CRSDs following mTBIs may improve our understanding of the nature of this association." (Ayalon et al., 2007, p. 1139)

Practice points	Research agenda
4. Proper diagnosis of CRSDs is important as a misdiagnosis of insomnia may lead to inappropriate prescription of hypnotic medication, which may help them to fall asleep, but will not be efficacious in normalizing the sleep-wake cycle (Ayalon et al., 2007, p. 1139)	
5. Treatments with melatonin or bright light may be more appropriate with CRSD	

2.3.2.3 Paediatrics

We identified six studies, five of which were of moderate quality, that reported sleep complaints in children and adolescents, and, five of these focused specifically on mTBI. In a 2001 study of 19 adolescents 3 years post minor head injury (mHI), Kaufman et al. (2001) reported that in comparison to healthy controls, head injured teens had significantly reduced periods of sleep time, total sleep time and sleep efficiency, as well as increased number and length of awakenings, objectively measured by PSG and actigraphy over 5 days. Subjectively, those with mHI reported significantly more difficulties falling asleep, difficulty waking in the morning, restless sleep and parasomnias, fearful awakenings from sleep and increased daytime sleepiness, than healthy controls. Further investigations by Pillar et al. (2003) found that in comparison to healthy controls, nearly one third (27/98) of the participants aged 8-18 years, with 0.5-6 years post-mHI had subjective complaints of sleep disturbance, and shorter weekend sleep time. The authors identified that those with mHI and complaints of sleep disturbance were also more likely to complain of bruxism and manifested a significantly greater BMI. Further, these individuals came from families with a lower level of parental education. While no information was available regarding pre-injury BMI, or any patterns of weight gain post-injury, the authors concluded that risk factors for sleep disturbance in mHI include heavier body mass and lower levels of parental education.

In 2004, Korinthenberg, Schreck, Weser, and Lehmkuhl examined predictive factors of post-traumatic syndrome in children (age range 3-13years) with mHI. The authors used data from EEG, in addition to a published neurological examination protocol, and a structured validated interview at two time points (T1: within 24 hours of the injury and T2: 4 to 6 weeks post-injury) to identify that at follow-up, 23/98 continued to present with psychiatric complaints including sleep disturbance and fatigue. These findings did not correlate with the severity of the injury, somatic, neurologic or EEG findings immediately post-injury. In their discussion, the authors state that the 'lack of a correlation with the acute concussional symptoms, acute neurological findings and the acute EEG abnormalities suggests that post-traumatic complaints in our patients are not primarily caused by organic structural or functional changes" (Korinthenberg et al., 2004, p. 116). They note that parental and patient anxiety is a frequent problem after even mHI, and it correlates with persistent symptoms.

In contrast however, Necajauskaite, Endziniene, and Jureniene (2005) studied 102 matched pairs of children aged 4-16 years of age, case group with mTBI and comparison group with mild bodily injury but no mTBI, and found that while 16.7% of the parents in the case group reported sleep disturbances in their children shortly after the trauma (exact time not defined), they did not find any significant differences in subjective reports of sleep disturbance between the two groups in the month prior to follow-up (1-5 years post-injury, mean = 27 months).

The most recent study to examine sleep in children with mTBI, Milroy, Dorris, and McMillan (2008) compared 18 children aged 7 to12 years, with mTBI with 30 children with orthopaedic injuries, average time post-injury 24 months. These authors used both subjective and objective measures (parental and self-report sleep questionnaires and actigraphy), and while parents reported greater sleep disturbances in the mTBI group, there were no significant differences between the groups with respect to daytime sleepiness, children's self-report of sleep disturbance and on actigraphy.

We found only one study which looked at sleep in children with moderate to severe TBI (modTBI to sTBI). Beebe et al. (2007) compared parental reports of sleep behaviours in

approximately 100 children, 50 with modTBI and 50 with sTBI aged 6 to12 years, with a comparison group of 80 children with orthopaedic injuries. The children were followed longitudinally over three time points, at approximately 6, 12, and 48 months post-injury. The authors reported that daytime sleepiness and nocturnal sleep duration were increased post-TBI (both groups). The modTBI group reported higher baseline sleep problems than the sTBI and the orthopaedic group, however this declined over the follow-up period (the specific time course was not specified) to a level consistent with the general population (6-9%). However, they reported that the sTBI group displayed an injury associated increase in sleep problems with the prevalence nearly doubling from 16% at baseline to 31% post-injury (again, specific timelines were not specified). The authors cautioned that these results should be considered as preliminary given the limitations of the outcome measure; however, they conclude sleep problems emerge after severe paediatric TBI (and are present in the post acute stage in modTBI).

In conclusion, there is emerging conclusive evidence to support the incidence and prevalence of sleep disturbances in children and adolescents post-TBI, across all levels of severity. There is both subjective and objective evidence documenting the prevalence of sleep disturbance in adolescents with mTBI several years post-injury. There is emerging subjective evidence to suggest that sleep disturbances become more prevalent over time in children with sTBI, yet decline over time post-injury in children with modTBIs. There is evidence to suggest that sleep problems in children with mTBI do not correlate with initial neurological findings. Clearly the research on sleep disturbances in children with TBI is in the early stage, and warrants further scientific investigation to more clearly identify the nature and patterns of the disturbance, any functional implications and appropriate interventions.

Table 8

Practice Points and Proposed Research Agenda: Paediatrics

Practice points	Research agenda
1. Children and adolescents with mTBI/mHI need to be systematically and routinely assessed for subjective complaints of sleep disturbances and followed up over time.	1. Sleep (and wake) problems in children and adolescents with both mild and moderate-severe TBIs should be evaluated longitudinally by both objective and subjective measures beginning at the onset of injury, to determine any patterns in the developmental course of sleep disturbance
2. Children with moderate-severe TBIs should be followed and assessed for emergence of sleep problems, with provision of appropriate sleep interventions.	
3. Adolescents with mHI, higher BMI and lower levels of parental education are at increased risk of sleep disturbances. Educating adolescents and parents about healthy eating and regular activity may be of benefit	
4. Providing parents with education and information during the acute stage post-mHI may help to alleviate anxiety and improve outcome	

2.3.2.4 Neuropsychological Implications

Sleep disturbances following TBI have been reported to exacerbate cognitive and behavioural sequelae. We identified four studies of moderate quality, three that evaluated neuropsychological (and cognitive-communication) function in relation to sleep disorders following TBI, and one that documented both sleep and neuropsychological sequelae following nonimpact brain injury. Henry, Gross, Herndon, and Furst (2000) retrospectively investigated the neuropsychological and behavioural functioning of 32 adults (aged 18-66 years) with "non-impact brain injury" (i.e., whiplash), up to 65 months post-injury. The authors used a comprehensive battery of standardized neuropsychological and psychological tests to assess cognition, motor skills and mood functioning. As the study was

retrospective, some participants had had structural neuroimaging, and three had undergone overnight sleep studies, in addition to neurological examination and interview. Results indicated that patients with whiplash injury demonstrated persistent cognitive, behavioural and emotional dysfunction years post-injury. Fifty–three percent had problems with sleep (not defined) in addition to difficulties with attention, concentration, executive functions, reduced information processing, word finding, sexuality, anxiety and depression. Of the 3 participants who underwent a nocturnal sleep study, sleep maintenance insomnia was identified with altered sleep stage percentages and altered REM rhythms. While the authors cite methodological limitations as precluding any conclusions regarding causation, the findings of sleep disturbance following whiplash are not surprising given the shearing injury and potential involvement of the hypothalamus.

In 2004, Mahmood et al. conducted an investigation of the relationship between sleep disturbance and neurocognitive ability in 87 adults with TBI across all levels of severity, who had been admitted to a comprehensive outpatient rehabilitation program. The authors conducted a cross sectional examination of scores on patients` neuropsychological examinations, the BDI-II and the PSQI. They reported that 'as would be expected, PSQI scores and BDI-II scores were significantly correlated because of the partial overlap of depression symptoms and insomnia" (Mahmood et al., 2004, p. 82). The authors also reported that measures sensitive to higher-order executive functioning and speed of information processing showed a positive relationship with PSQI scores. Their findings supported a hypothesis of a predictive relationship between performance on neuropsychological tests and reports of sleep disturbance in adults with TBI.

In 2007, Wilde et al. examined the impact of co-morbid OSA (diagnosed after the TBI) on the cognitive functioning of 19 patients with TBI, in comparison to 16 patients with TBI but without OSA. The participants were otherwise comparable in terms of age, education, injury severity, time post-injury and GCS (where available). The patients with TBI with OSA performed significantly worse on verbal and visual delayed recall measures, and had more attention lapses than the TBI without OSA patients. Interestingly, they did not differ on other measures of visual construction, motor and attention tests. The authors concluded

that TBI with OSA is associated with greater impairments in sustained attention and memory than those patients with TBI without OSA.

Wiseman-Hakes and Murray (2008) assessed daily self-and clinician-(rehabilitation worker) report of changes in cognitive and communication functioning, including sustained auditory attention/vigilance, speed of language processing, verbal memory and communication, in response to a course of pharmacological intervention phased in over 17 weeks, for post-traumatic hypersomnia. The self-report measure used in this study is the newly developed Daily Cognitive-communication and Sleep Profile, DCCASP, which is currently undergoing reliability and validity testing (Wiseman-Hakes & Murray, 2008). This case study participant was a young man in his late teens 11 months post severe TBI (sTBI), when the study began. As treatment progressed, the authors found a clear positive relationship between improved quality of sleep and language processing, (defined as the ability to follow and participate in conversation), sustained attention/vigilance (defined as the ability to pay attention and concentrate over time), and memory, (defined as the ability to remember things you have heard, done or seen). This was seen across the different phases of the medication regime ($p < 0.01$). A follow-up conducted at 3 years 8 months indicated that the gains in sleep, daytime wakefulness and cognitive-communication function had been maintained. Although the data were limited to one subject, the findings suggest that appropriate, timely and effective diagnosis, and management of sleep/wake disturbances post-TBI, may facilitate improved cognitive-communication function. The authors concluded that their results need to be corroborated with a larger sample size, and the addition of standardized neuropsychological and cognitive-communication assessment measures to clinically evaluate reported functional changes (Wiseman-Hakes & Murray, 2008). Please refer to Table 9 for identified practice points and a proposed research agenda for neuropsychological implications.

Table 9

Practice Points and Proposed Research Agenda: Neuropsycholgical Implications

Practice points	Research agenda
1. Comorbid sleep disturbances, particularly OSA can exacerbate cognitive deficits in verbal and visual delayed memory and sustained attention. Thus, effective diagnosis and management may improve cognitive function.	1. 'Further research should explore the thresholds at which sleep disturbance adversely affects cognitive function in persons with TBI' (Mahmood et al., 2004, p. 389)
2. Appropriate and timely assessment and treatment of post-traumatic hypersomnia may facilitate improvements in self-report of cognitive and communication function.	2. A prospective longitudinal study examining the interactions between injury severity, duration of post-injury recovery and its effect on the relationship between sleep morphology and cognitive function is warranted 3. A prospective longitudinal study of objective and subjective measures of cognitive-communication function in response to treatment of sleep and wake disturbances post TBI, using a larger sample size is warranted.

2.3.2.5 Intervention

The literature on treatment for/of sleep disturbances following TBI is relatively limited at this time. This may be a reflection of the complexity of this disorder from a number of perspectives; that is, lack of a clear aetiology in many patients, mixed diagnoses, lack of consistency regarding the developmental course of the disorder, and interactions with secondary issues such as pain and depression. We identified six papers for review in total; four were of moderate quality and two of high quality. Four of the six focused upon pharmaceutical management, and of these four, one was for the treatment of fatigue and excessive daytime sleepiness post-TBI, one was for the treatment of narcolepsy, another was for the treatment of insomnia following TBI and stroke, and only one addressed treatments for a number of different types of sleep disorders commonly associated with TBI. The remaining two papers focused on behavioural intervention specifically for insomnia.

These latter two papers of moderate quality by Ouellet and Morin (2004, 2007) assessed the efficacy of a protocol of CBT administered by a registered clinical psychologist over a period of 8 weeks. The first paper reports on an individual case study, and the second reports a single case series. The authors state that cognitive therapy for insomnia consists of 'identifying, challenging and altering a set of dysfunctional beliefs and attitudes about sleep', with the objective of 'breaking the cycle of insomnia; dysfunctional thoughts and emotional distress that lead to further sleep disturbances' (Ouellet & Morin, 2004, p. 1299). The authors do a thorough job of delineating the treatment protocol, which was adapted to take into account the deficits in memory, attention, and processing that can occur post-TBI.

The results of the case study are promising in that the participant experienced reduced sleep onset latencies, nocturnal awakenings, and an increase in sleep efficiency. These results were well maintained at follow-up at both 1 and 3 months. The authors built upon these initial results by expanding their assessment measures and number of participants in a single-case series of 11 individuals (6 males, 5 females) with mild to severe TBI. There are a number of relative strengths of this paper despite its small sample size. Participants were recruited from a variety of locations and methods including major rehabilitation centres across Quebec, Canada, as well as through advertisements to TBI associations and local support groups. Further, all levels of severities were represented, indicating that although the sample size is small, their sample is likely fairly representative of the post-TBI population. Their results indicated a decline in total overnight wake-time relative to baseline, as well reduction in overnight sleep variability in 8/11 participants. Treatment effects were seen 1 to 2 weeks after the beginning of therapy. All participants increased their sleep efficiency, and 5/11 achieved a sleep efficiency of greater than 90% at the 3-month follow-up. At post-treatment, 7/11 no longer fulfilled the diagnostic criteria for insomnia. Based on their results, the authors suggest that insomnia associated with TBI can be successfully improved in a large proportion of cases with short-term cognitive behavioural intervention.

The remaining four papers for review addressed pharmacological intervention. Jha et al. (2008) examined the efficacy of modafinil in treating fatigue and excessive daytime

sleepiness in individuals with TBI. This high quality, comprehensive and well-conceived study consisted of a double blind placebo cross over trial in which 53 patients with TBI were randomly assigned to receive up to 400mgs of modafinil, or equal number of inactive placebo tablets. The participants were a minimum of 1-year post-injury, with a severity level such that they required inpatient rehabilitation (no other information regarding levels of severity was provided). For the modafinil regime, patients took 100 mg (one tablet) once per day at noon for 3 days, and then increased to 100mg 2 times per day for the next 11 days, followed by the maintenance dose of 200 mgs twice daily in the a.m. and at noon. Following the end of the randomized study, both groups were offered a 4-week open label period where they could receive modafinil using individually clinically monitored titration and maintenance dosage. However, results indicated that after adjusting for baseline scores and period effects, there were no statistically significant differences between improvements with modafinil versus placebo on any of the outcome measures, (Fatigue Severity Scale, the Modified Fatigue Impact Scale and the ESS). Thus, despite the scientific rigor of this study, there were no consistent and or persistent clinical improvements.

The next study by Shan and Ashworth (2004) focused specifically on insomnia post-TBI and stroke, and aimed to compare the efficacy of lorazepam and zoplicone as treatment options. This study also followed a double blind cross-over trial involving 18 patients in total with TBI or stroke (six TBI, six right hemisphere and six left hemisphere stroke, no information as to severity or time post-injury). Participants were prescribed either lorazepam 0.5-1.0mgs at bedtime as needed X7 days followed by zoplicone 3.75-7.5mgs at bedtime, also as needed. Participants were able to regulate their own dosage from 0- ½ - 1 tablet per night, to 'empower them and to simulate what normally happens on our ward.' [67] (Shan & Ashworth, 2004, p. 422) Results indicated no significant differences on total sleep time, or in subjective measures of sleep. Further, they evaluated cognition using the mini mental status exam (which in our view is an extremely weak and insensitive measure for this purpose, particularly for the TBI population), and found no changes with either medication. The authors concluded that zoplicone and lorazepam are equally effective in the treatment of insomnia for both populations. However, as they do not report any

baseline information on sleep, the reader is not able to determine any actual level of improvement, thus negating any clinical application of their findings; another weakness of this study.

The most recent study by Castriotta et al. (2009) aimed to determine whether treatment of specific sleep disorders (which they diagnosed by means of PSG) would result in resolution of those disorders and improvement of symptoms and daytime function. The investigators conducted a thorough high quality prospective evaluation of 57 unselected patients with TBI, > 3 months post-injury with PSG, MSLT, ESS and neuropsychological testing including the Psychomotor vigilance test, (PVT), Profile of Mood States, (POMS), and the Functional Outcome of Sleep Questionnaire (FOSQ), prior to and after treatment for OSA (23% of 22/57), post-traumatic hypersomnia (PTH) (3%), narcolepsy (5%), PLM (7%), and objective excessive daytime sleepiness (22%). In total, 22/57 participants had abnormal polysomnograms (39%). Treatments included continuous positive airway pressure (CPAP) for OSA, modafinil (200mgs) for narcolepsy and PTH, or pramipexole (0.375mg) for PLM. In terms of response to treatment, the investigators found that the apneas (and hypopneas, as well as snoring) were eliminated by the CPAP; however there was no significant change in MSLT scores. Additionally they found that PLM were eliminated with pramipexole. One of 3 participants with narcolepsy and 1 of 2 with PTH had resolutions of hypersomnia with modafinil. However, there were no significant changes in FOSQ, POMS, or PVT results after treatment. The authors concluded that treatment of various sleep disorders after TBI may result in polysomnographic resolution, without change in sleepiness or neuropsychological function.

Overall, the results of these four studies on pharmacotherapy leave us with somewhat of a clinical conundrum. Castriotta et al.'s (2009) results may provide guidance to those treating post-traumatic apnea (and hypopneas), PLMs and hypersomnia. This makes intuitive sense from a clinical perspective, as these disorders are relatively more "clear cut" in their aetiology. Insomnias however, can be more complex and multi-faceted in their aetiology, potentially including a combination of underlying physiological and psychiatric issues, and thus are often harder to manage pharmacologically without a combination of

medications. Further, results of the Shan and Ashworth (2004) study lead us to conclude that standardized dosages may not be effective, and that any medication regime needs to fine tuned to the individual needs of the patient, an important protocol built into the final 4 weeks of the Jha et al. (2008) study. Thus an ideal treatment regimen may include a trial of cognitive behaviour therapy, with the addition of pharmacotherapy as needed, specifically tailored to the individuals' symptoms, body weight and tolerance. Additionally, Castriotta et al.'s (2009) report that resolution of polysomnographic findings without associated improvements in daytime function suggests that a follow-up study may be of benefit, with an individual case series design where additional treatments and or medications could be added, specific to each participant. Based on the current findings to date it is clear that intervention for sleep and wake disorders post-TBI is an area of significant need with respect to future research directions.

Table 10

Practice Points and Proposed Research Agenda: Intervention

Practice points	Research agenda
1. Cognitive-behavioural therapy is a promising alternative and or adjunct to pharmacotherapy for the treatment of insomnia post-TBI.	1. Does treatment using individualized dosages and or a combination of medications specific to unique the needs of each individual patient result in improvements in sleep symptoms and daytime function?
2. A standardized dose of modafinil is not effective in addressing daytime sleepiness. Dosage should be fine-tuned according to the individual needs of the patient.	

2.4 Discussion

This systematic review was conducted to summarize the current literature on the topic of sleep and wake disorders following traumatic brain injury, and to critically appraise the research directions. In summary, our findings concur with previous reviews in that sleep

and wake disorders are a prevalent and complex sequelae of TBI occurring at all stages across the continuum of recovery from acute, to post-acute, to rehabilitation, in both children and adults, and for a number of patients, continuing for many years post-injury, long into the community. These disorders are complex and multi-factorial, impact on neuropsychological functioning, participation in rehabilitation and quality of life. They may evolve from a neurophysiological disruption in brain function to a secondary disorder associated with depression, anxiety, weight gain and other factors. As such, intervention is equally complex and much more work needs to be done to fully understand the underlying aetiologies and to find appropriate treatments. With regards to methodological quality and scientific rigor of the literature, there is a readily observable trend towards higher quality more methodologically sound studies as the literature evolves over time. To date, however, most studies have been limited by small sample sizes, large ranges in time post-injury of participants, loss to, or lack of follow-up and sample bias due to timing and methods of recruitment. Thus it is still unclear exactly whom of the TBI population are affected, and how the disorder evolves over time. Further, it is unclear why those with mTBI are more likely to present with insomnia or symptoms of insomnia, and whether or not this is a true manifestation of the disorder, or a reflection of other issues such as self-awareness, the challenges of returning to work, school and community and such. We recognize however, that the current state of the literature is also reflective of the inherent complexities of conducting clinical research with this highly diverse, heterogeneous population.

2.4.1 Limitations

Although this current review utilized a systematic approach for the critical appraisal and determination of methodological quality of the literature, we recognize a number of limitations in this methodology. All of the papers included have been peer reviewed, and as such, there is publication bias. Further, while we have attempted to fully capture all of the recent relevant articles with our search criteria, it is possible that we may have missed papers and as such, this review may not be fully representative of the current literature. Given constraints of time, we did not contact any of the study authors directly to clarify any points of confusion, and as such, our quality rating system is based upon our understanding

of the reporting of the methodology and results and thus may not be truly representative of the actual study design and quality.

2.4.2 What This Paper Adds

Despite the limitations of this review, this paper adds to the body of knowledge regarding sleep and wake disorders following TBI. To date, it is the most comprehensive review, with the inclusion of literature specific to the paediatric population, and is also the first to attempt to delineate the prevalence and nature of sleep disorders by timing of recruitment and levels of severity across the continuum of recovery. It is also the first review to critically appraise the methodological quality of the current literature.

2.5 Conclusions and Future Research Directions

Sleep and wake disorders following traumatic brain injury have received increasingly considerable attention amongst the clinical and scientific community. Researchers have attempted to quantify the incidence and prevalence of these disorders, and to define and describe the nature of the disorder with both subjective and objective measures. Further, attempts have been made to understand the underlying pathophysiological mechanisms and other contributing factors as well the functional implications, and treatment options. However, much further work is needed to fully understand this complex disorder and to identify appropriate and timely interventions. What is needed is a large multi-centre study which follows all those with TBI from the acute stage with regular follow-up into the community, such that results can be reliable, valid and stratified by nature and severity of injury, age, sex, imaging results, and development of the disorder over time. Additionally, we recommend that outcomes for either epidemiological or intervention studies should also capture functional outcomes in addition to sleep measures and cognitive measures to fully assess the impact of the intervention. Finally, we concur with Dr. Richard Castriotta (2008) who stated in the editorial entitled “Collaboration in research involving traumatic brain injury and sleep disorders” that “Careful study will require much effort and many resources, which can best be brought to fruition through collaborative efforts across multiple centres, with an aim to elucidate the causes, foster early diagnosis, and develop optimal treatment for these problems” (Castriotta, 2008, p. 177). These continuing efforts

will further inform clinical practice and ultimately contribute to the development of practice guidelines for the systematic evaluation and treatment of sleep and wake disorders following TBI.

Chapter 3
Impact of Post-Traumatic Hypersomnia on Functional Recovery of Cognition and Communication: A Case Study[2,3]

3. Abstract

Primary Objective: To illustrate how a comprehensive, longitudinal approach to management of post-traumatic hypersomnia and mood disturbance can positively impact recovery of cognition and communication. **Research Design**: A single case study; pre–post intervention. **Methods and Procedures**: The male participant sustained a severe TBI and subsequently developed cognitive- communication impairments, sleep and mood disturbance, and excessive daytime sleepiness. Sleep and wakefulness were assessed by Clinical Interview, Polysomnography, Multiple Wake Test (MWT), Epworth and Stanford Sleepiness Scales, and The Daily Cognitive-Communication and Sleep Profile (DCCASP). Cognitive-communication (alterations in communication due to underlying deficits in cognitive processes) was also assessed by the DCCASP. A separate analysis of cognitive functions was undertaken by standardized clinical neuropsychological assessment. Sleep, wake and mood difficulties were pharmacologically managed. **Main Outcomes and Results**: Baseline polysomnography indicated mildly abnormal sleep and a subsequent MWT revealed an inability to maintain alertness. There was a clear positive correlation between perceived quality of sleep, and language processing, attention, and memory, seen across the phases of the medication intervention ($p < 0.0001$). **Conclusions:** A pharmacological management program addressing the multi-factorial underlying aetiology

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was successful in improving sleep, alertness and mood. These findings suggest that treatment of sleep/wake disturbances and mood following TBI is a complex undertaking. However, successful, management may facilitate improvements in cognitive-communication function.

Key words: sleep disturbance, hypersomnia, excessive daytime sleepiness, traumatic brain injury, cognition, cognitive-communication, mood disturbance.

3.1 Introduction

Traumatic brain injury (TBI) is the leading cause of death and disability for those under the age of 45 in North America. Given that the peak age of injury occurs between the ages of 15-24 years, and the majority of individuals are aged 45 and under, this has significant implications to society as these young people are left with chronic residual neuropsychiatric, cognitive and communication disabilities (Seyone & Kara, 2006). Impairments in sleep and the development of sleep disorders such as insomnia, fatigue and excessive daytime sleepiness are among the most commonly reported neuropsychiatric sequelae (Seyone & Kara, 2006).

Studies conducted amongst heterogeneous samples of individuals with TBI report an incidence of sleep disorder that varies from 30-70% during the first 3 months post-injury and a prevalence up to 73% long past the injury (Colantonio, Ratcliff, Chase, & Vernich, 2004); approximately 30% meet the DSM-IV criteria for insomnia (Burke et al., 2004; Castriotta et al., 2007; Fichtenberg et al., 2002; Makley et al., 2008; Ouellet et al., 2004; Wiseman-Hakes et al., 2009). This is in contrast to the incidence of sleep disorder reported in the general population, which is approximately 10% for those meeting DSM-IV criteria (Morin, LeBlanc, Daley, Gregoire, & Mérette, 2006; Roth, 2007). Recent data (Castriotta et al., 2009) indicate that among survivors of traumatic brain injury across a range of severities, (N = 57), 30% with severe TBI (GCS <9), 5% with moderate or severe TBI, 18% with moderate TBI (GCS 9-12, or GCS 13-15 with positive CT findings) and 9% with mild TBI (GCS 13-15 and negative CT findings), 39% had abnormal sleep studies. Specifically, 13% had obstructive sleep apnoea, 7% had periodic leg movements 3% had post-traumatic hypersomnia, 21% had objective excessive daytime sleepiness and a further 5% had post-

traumatic narcolepsy. This is not surprising as TBI is often associated with a reduction in CSF orexin/hypocretin which is a primary pathological feature of narcolepsy (Baumann et al., 2005). Similar findings of sleep disorders other than insomnia following TBI have also been reported by Verma et al. (2007). Abnormal sleep patterns post-TBI, including difficulty falling or staying asleep and excessive daytime sleepiness, can exacerbate other difficulties associated with the injury. These may include pain, mood, behavioural, cognitive and communication disturbances such as increased difficulty with new learning (Baumann et al., 2007; Castriotta et al., 2007; Mahmood et al., 2004). A recent systematic review of the literature pertaining to sleep and traumatic brain injury (Wiseman-Hakes et al., 2009) reported that depression and anxiety have been identified as risk factors for sleep disturbances, particularly insomnia. The authors of this review concluded that sleep disorders may be confounded over time by the subsequent development of depression and anxiety, making it difficult to draw specific conclusions regarding the aetiology of these disorders (Wiseman-Hakes et al., 2009).

Impairments in cognitive-communication abilities are also common sequelae of TBI, and occur at a frequency of 81% in the acute stage (MacDonald & Wiseman-Hakes, 2010). Cognitive-communication disorders are defined as alterations in communication due to underlying deficits in a variety of linguistic and nonlinguistic cognitive processes, as a result of neurological impairment. Deficits post-TBI typically include impairments in sustained and complex attention, verbal memory, efficiency and speed of language processing, pragmatics and impairments in new learning which impact listening, speaking, reading, writing, conversation, and social interaction (Hartley, 1995; MacDonald & Wiseman-Hakes, 2010). Examples of resulting communication deficits include difficulties attending to and understanding conversation (particularly fast paced multi-person conversations), difficulties interpreting subtleties and humour, and problems understanding complex written language and following complex commands. Other examples include difficulties following and retaining information from a story, and with organization of spoken expression so that it is coherent and succinct, and difficulty responding efficiently and appropriately in conversation. These difficulties have a significant impact on social interaction and ultimately on community reintegration. In fact, the literature on long-term outcomes following TBI, emphasizing those sequelae which

translate into barriers to successful rehabilitation and community re-integration, indicate that ineffective interpersonal communication skills are a major contributing factor to poor long-term outcome (Hartley, 1995; MacDonald & Wiseman-Hakes, 2010).

The link between sleep and cognition has been well documented in the literature (Giglio et al., 2007; Maquet et al., 2003; Stickgold, 2003a, 2003b; Stickgold & Walker, 2007). This body of research emphasizes the crucial need for successful management of sleep/wake disturbances following TBI, in part to optimize the rehabilitation of cognition and resulting cognitive-communication impairments, thus potentially improving functional communication in survivors of TBI. Some initial research has looked at the relationship between sleep and cognition in survivors of TBI. Results of these studies report greater impairments in sustained attention, memory, higher order executive functions and speed of information processing in patients with TBI and sleep disturbances in comparison to patients with TBI without sleep disturbances (Castriotta et al., 2009; Mahmood et al., 2004; Makley et al., 2009; Wilde et al., 2007).

Despite the prevalence of sleep/wake and cognitive-communication disturbances post-trauma, the inter-relationship between the two has received little scientific attention to date. In this study we evaluated the impact of effective pharmacological management of sleep/ wake and mood disturbance on self- and clinician-reports of attention, memory, speed of language processing and mood in a patient with severe TBI. Evaluation was completed via the Daily Cognitive-communication and Sleep Profile.

3.2 Methods

3.2.1 Ethics

The participant provided written informed consent to allow his case details to be presented for publication, consistent with the guidelines of our hospital ethics review board.

3.2.1.1 Participant History

3.2.1.1.1 Description of injury

The participant was a young man in his late teens who had been attending high school and was an accomplished high-level extreme sports athlete pre-injury. His prior medical history

was relatively unremarkable, although there were reports of substance abuse including some binge drinking on the weekend and occasional recreational drug use. He had no prior history of brain injury or neurological disorder, and no history of learning disability or psychiatric disorder. Further, he and his family did not report any pre-injury sleep difficulties. He sustained a severe traumatic brain injury as the result of a motor vehicle collision (MVC) as the unbelted driver of a vehicle that lost control after hitting a patch of ice. The vehicle was hit by an oncoming car and the participant was ejected through the passenger window. His initial Glasgow Coma Scale (GCS) score at the scene was 3/15.

3.2.1.1.2 Initial CT scan results

An initial CT scan taken the day of the MVC revealed small amounts of subarachnoid blood around the sylvian fissures, particularly in the right frontal area. There was blood in the third ventricle and lateral ventricles bilaterally, basilar frontal lobe contusions and hemorrhagic regions in the basal ganglia. There was a hyper-density in the right cerebellum, and mass effect causing mild deformity of the fourth ventricle.

Pattern of Cognitive Recovery

Acute care. The participant remained in a coma for 26 days, and 1 month post-injury he presented as confused and agitated with ongoing post-traumatic amnesia, and required maximal assistance for all activities of daily living.

Inpatient rehabilitation. He was transferred to an inpatient rehabilitation centre 3 months post-injury. He remained confused, highly agitated and disoriented with severe attention impairments and a working memory span of 3-5 minutes. His sleep was fragmented and disrupted with night time arousals. He was easily fatigued and presented with an inconsistent pattern of information and language processing throughout the day. An initial neuropsychological evaluation was conducted prior to discharge from inpatient rehabilitation at 8 months post-injury. Results of that evaluation were reported as showing average intelligence, but borderline auditory and visual-motor processing under timed conditions, poor sustained attention and long-term memory as well as difficulties with processing and retrieving information. He also exhibited high levels of frustration and fatigue, with poor attention after an hour.

Community reintegration. The participant was discharged home 10 months post-injury to live with his mother. His medication at discharge included zopiclone, which was prescribed by his physician at the time for sleep difficulties. He was purposeful and appropriate, with some emotional lability, requiring 24-hour per day attendant care and a 1:1 rehabilitation coach during the day. His language processing had improved; however, he remained highly susceptible to fatigue, with continued attention and memory impairments. He returned to high school in 12th grade for two classes with 1:1 support, and continued with an intensive community-based rehabilitation program including occupational therapy, physiotherapy, speech language pathology and social work counselling. During this period, two neuropsychological evaluations were performed for clinical rehabilitation purposes separate from the sleep treatment, at approximately 19 months and 31 months post-injury to guide and monitor his recovery (see Table 11).

Table 11

Highlights of Neuropsychological Findings Regarding Cognitive Communication Sub-Skills

Neuropsychological test	19 months post-injury score (T-score)*	31 months post-injury score (T-score)*
Intelligence/Language Tests:		
Wechsler Adult Intelligence Scale III		
FSIQ stand. score	94 (46)	100 (50)
VIQ stand. score	91 (44)	98 (48)
PIQ stand. score	98 (48)	102 (52)
Comprehension subtest stand. score	8 (43)	9 (47)
Similarities subtest stand. score	11 (53)	12 (57)
Wide Range Achievement Test – III –		
Arithmetic stand. score	75 (34)	70 (30)
Controlled Oral Word Association FAS -total	39 (51)	36 (49)
Boston Naming Test-total	55 (40)	----
Attention, Information Processing, Working		
Memory Tests:		
Trails A – time	28 (44)	31 (44)
Trails B - time	87 (41)	92 (36)
Digit Span subtest	8 (43)	10 (50)
Letter Number Sequencing subtest	10 (50)	12 (57)
Spatial Span subtest	11 (53)	11 (53)
Verbal Memory Tests:		
WMS-III Auditory Immediate	80 (37)	99 (49)**
WMS-III Auditory Delayed	58 (21)	71 (31)**
WMS-III Auditory Recognition	55 (20)	90 (43)**
California Verbal Learning Test-II - total	36 (32)	46 (46)**
Abstract Reasoning Test:		
Category Test-total errors	54 (39)	30 (48)**
Depression/Anxiety:		
Beck Depression Inventory –II – total	18 (mild-mod level)	12 (minimal level)**
Beck Anxiety Inventory – total	11 (mild level)	4 (minimal level)

Note. *all scores presented as T-scores for ease in comparison; $\bar{x}$ = 50, sd = 10
**represents a clinically significant improvement on the neuropsychological test

Sleep and cognitive-communication function. At approximately 11 months post-injury (335 days), the participant's sleep had deteriorated markedly with his medication at the time, such that he was reporting significant difficulties falling and staying asleep. His daytime sleepiness impaired his ability to participate in therapies and attend school several times per week. He exhibited notably increased anxiety, irritability and perseveration, and reduced conversational abilities and communication competence. During the clinical interview, he reported that he went to bed between 11pm-12am, took on average 45 minutes to 1 hour to fall asleep, awoke 3-4 times per night, and had difficulty falling back to sleep. He was awakened with assistance at 7:30am. This was corroborated through daily reporting on the Daily Cognitive-Communication and Sleep Profile (DCCASP; see Measures).

3.3 Measures

Sleep and wakefulness were formally evaluated with the Epworth Sleepiness Scale (ESS) (Johns, 1991), the Stanford Sleepiness Scale (SSS) (MacLean, Fekken, Saskin, & Knowles, 1992), polysomnography and Maintenance of Wakefulness Testing (MWT) (Doghramji et al., 1997). As self-report of sleep, wakefulness and daytime function are also important components of any assessment and management program, the DCCASP was also administered (see Appendix S). The Daily Cognitive-Communication and Sleep Profile (DCCASP) is a series of seven self-report five-point Likert rating scales developed for use in clinical practice and as a research tool, as a means of monitoring daily fluctuations in cognitive-communication function in relation to quality of sleep. The measure was developed by Wiseman-Hakes and is readily available for use upon request. It was developed to fill a gap in available measures designed to evaluate sleep function by self-report, and the impact of sleep (or lack thereof) on daytime function.

While the Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) has been validated for use with a traumatically brain injured population, it requires the respondent to recall and rate their sleep retrospectively over the last month (Fichtenberg, Putnam, Mann, Zafonte, & Millard, 2001). Given that many individuals with TBI have difficulties with memory, and, the fact that sleep (and thus daytime function) can

change many times over the course of a month, a measure that only requires the respondent to recall for 1 day is more likely to be sensitive and accurate. Further, information regarding sleep and daytime function on the PSQI is limited to one question, which asks if the person has had 'any problems keeping up his/her enthusiasm to get things done'. In contrast, the DCCASP asks the individual to specifically consider and rate his/her functional performance daily across seven domains of sustained attention/vigilance/executive attention to spoken or written communication, verbal memory (retention of spoken or written information), speed of language processing, sleep quality, level of fatigue, daytime sleepiness, and mood (see Table 12). Thus DCCASP provides specific and detailed formation about function and may provide guidance to inform treatment decisions.

Table 12

Abbreviated DCCASP-Version 1

Item	How was your **Sleep Quality?**						
Scale	1 Worst Possible Sleep	2	3	4	5 Best Possible Sleep		
Day*	SUN	MON	TUES	WED	THU	FRI	SAT
Rating*	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)
Item	How was your Mood today?						
Scale	1 Overall anxious, irritable, unhappy, restless, and easily annoyed, overwhelmed by my day	2	3	4	5 Overall calm, reasonably content, able to handle what the day threw at me		
Item	How Tired did you feel today?						
Scale	1 Good level of energy, able to stay awake with no difficulty	2	3	4	5 I felt really tired, low energy, fell asleep during the day		
Item	Rate your Attentiveness and Concentration for today.						
Scale	1 I couldn't concentrate today and I couldn't block out things that distracted me	2 Really hard to pay attention. I kept focused briefly but got distracted	3 Hard to pay attention but I can follow tasks and get back on track if distracted. May need help to get refocused	4 Some difficulty paying attention and following tasks. I occasionally have to get back on track if distracted	5 Fairly easy to block out distractions, I can pay attention for extended periods of time		

Item	Rate your Memory abilities for today				
Scale	1	2	3	4	5
	Can't remember activities, events, or conversations from today	If reminded, can remember the gist of some activities, events, or conversations from today	With no reminders can remember the gist of some activities, events, or conversations from today	Can remember several details of activities, events, or conversations from today	Can remember almost all the details of activities, events, or conversations from today
Item	Rate your Communication and Conversation abilities for today.				
Scale	1	2	3	4	5
	I was unable to carry on a conversation today. My conversation partner must always speak slower and simplify the topic	I could carry on a conversation with one person, but need extra time to think and respond. At times conversation partner must speak slower and simplify the topic	Able to converse with one person, if he/she speaks slower. Can carry on multi-speaker conversations briefly if topic stays the same, but I need extra time to think and respond	Can carry on a conversation with one person, conversation partner doesn't need to speak slower. Some difficulty following and responding to multi-speaker conversations, but I can do it	Can keep up with and reply to a multi person or single person conversation with minimal difficulty

Note. * The "Day" and "Rating" rows following each "Scale" row but for space considerations they have not been repeated for each Item in this table.

The DCCASP is a monitoring profile only; there is no composite score, and it is not meant to have normative comparison data. Despite its lack of psychometric properties at this time, pilot testing has found it to be sensitive to subtle changes in sleep and daytime function in a clinical setting, and useful in educating patients and identifying sleep patterns and trends. It can be completed either by the participant, therapist or significant other who has the opportunity to observe the participant over the course of the day. This represents the first empirical examination of the DCCASP and its ability to monitor changes in sleep function.

3.4 Data Collection Protocol

At baseline assessment, approximately 12 months post-injury the participant underwent polysomnography at a local sleep clinic, and completed the ESS and SSS subjective measures. Using the DCCASP the participant, with assistance from a rehabilitation worker, began keeping a daily record for the next 17 weeks of bed time, approximate time to fall asleep, number of night time awakenings, subjective perception of sleep quality, daytime fatigue and sleepiness including naps, and subjective perception of cognitive-communication function including sustained attention/vigilance, language processing (ability to follow and participate in conversation), and verbal memory. His subjective perception of mood was also reported.

A follow-up interview was completed at 3 years 8 months by a diplomate of the American Board of Sleep Medicine after many medications had been tried. At that time the participant underwent polysomnography and MWT, consisting of four 40-minute opportunities to resist sleep at 2-hour intervals in the daytime.

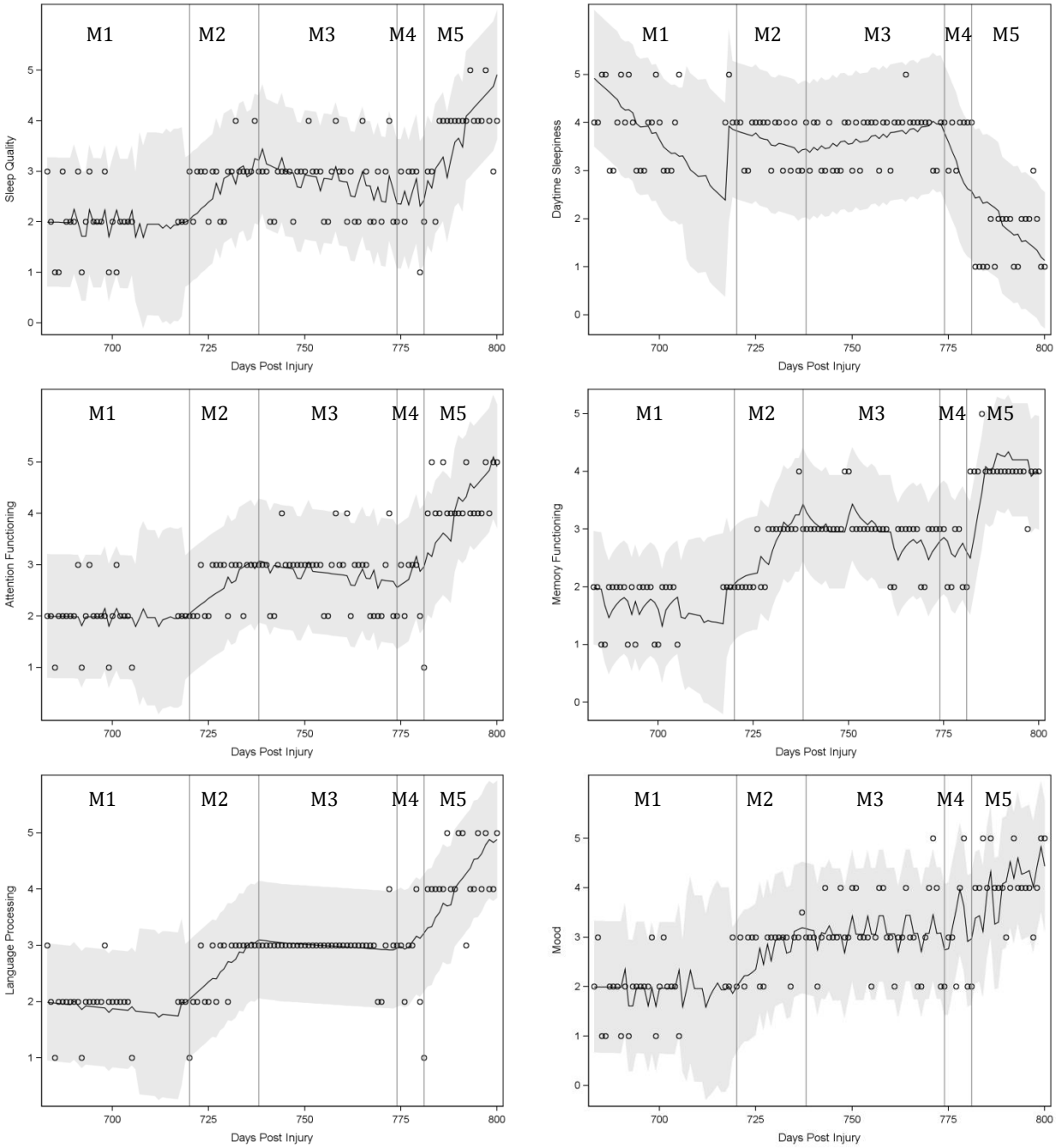
3.5 Treatment

Treatment consisted of pharmacological management by other physicians. At baseline the participant had been directed to implement a sleep hygiene routine that included maintaining a regular bedtime, ensuring that the room temperature, mattress, pillow and bedclothes were comfortable and that the computer and any music devices were turned off. He was also taking zoplicone 7.5mg nightly (M1). Zopiclone is a sedative with a pharmacologic profile similar to that of benzodiazepines in that it reduces sleep onset

latency (Repchinsky, 2010). Zoplicone is not currently available in the United States, but an enantiomer is in wide use.

As part of the study, the pharmacological management was altered; however, the sleep hygiene strategy was maintained. Immediately after baseline data collection (at 12 months post-injury), zopiclone was replaced with lorazepam 1 mg, and citalopram 20 mg (M2). According to Flanagan, Greenwald, and Wieber (2007) many benzodiazepines, particularly those with long half-lives, can have undesirable 'hang-over' side effects the day after ingestion. Citalopram has been found to have a REM (rapid eye movement) suppression effect during sleep, consistent with many selective serotonin reuptake inhibitors (SSRIs) (Winokur et al., 2001).

These medications were maintained for a month at which point the citalopram dosage was doubled to 40mg (M3). A further month later (14 months post-injury) methylphenidate 20mg was added (M4), and then 1 week later increased to 40mg daily (M5). Methylphenidate is a stimulant which enhances catecholaminergic activity, and is commonly administered to address fatigue and reduced arousal in individuals with TBI (Fellus & Elovic, 2007; Gerard & Ivanhoe, 1996; Levine & Greenwald, 2009). Thus, for the duration of the study, the participant underwent five medication adjustments (M1 = baseline; see Figure 3). At follow-up, at 3 years 8 months, the participant was still taking lorazepam and citalopram, but modafinil was substituted for methylphenidate, and mirtazapine had been added. Modafinil is a wake-promoting agent that acts somewhat differently than classic stimulants in that it is less likely to cause psychomotor agitation (Fellus & Elovic, 2007). Flanagan et al. (2007) reported that mirtazapine has been shown to improve sleep onset latency and total sleep time without alterations in sleep architecture, in individuals with major depression.



Legend: Open circles represent observed values, solid line represents predicted values, shaded areas represent 95% confidence interval for predicted values. M1 – M5 represent time period of five different medication regimens as described in methods. In all domains except daytime sleepiness a "1" represents a rating of poor outcome and a "5" represents a rating of the best outcome. For daytime sleepiness a "1" represents a rating of the best possible outcome and a "5" represents a rating of the least desirable outcome.

Figure 3. **Time series analysis of DCCASP scores.**

3.6 Analysis

An interrupted time-series analyses (ARIMA models) approach was used to examine the effect of medication regimen on cognitive communication function as measured by the DCCASP and sleep quality over time. Time series analysis is a technique used to handle repeated measures of single subject data where the measures are taken at regular (or nearly equal) intervals of time. This approach has been found to be useful for studies in health care settings, and for preliminary studies such this N-of-1 case study (Crabtree, Ray, Schmidt, O'Connor, & Schmidt, 1990; Smith, Handler, & Nash, 2010). This N-of-1 case study is similar to many time series analyses where the patient is 'the system'. Where there are sufficient repeated observations (10-50) for each treatment condition, a time series is an appropriate approach. In fact, 'with a long baseline and outcome series, statistically rigorous internal validity (a change in level or trend), can be detected in a single 'system', which in this case, is the participant (Crabtree et al., 1990).

In this context (i.e., an N-of-1 study using a newly developed tool, the DCCASP, and the relatively small sample of data points), the time series analysis, was performed as to serve as a visual tool used to summarize and visualize changes in sleep pattern as they relate to changes in medication regimen through graphical representation of predicted values and 95% confidence bands. Sample autocorrelations and Box-Ljung Q tests for the first 24 lags showed that the model had residuals consistent with white noise

Changes in sleep outcomes over time were related to changes in medication regimen to identify whether changes in medication regimen had no effect, abrupt and sustained, gradual and sustained, abrupt and diminishing, or gradual and diminishing effects. All analyses were conducted with SAS v9.2 (SAS Institute Inc., 2008).

3.7 Results

3.7.1 Sleep Findings

The sleep studies were scored before new rules were provided by the American Academy of Sleep Medicine for collection and scoring of sleep studies and were therefore scored using conventional Rechtschaffen and Kales criteria (Iber, Ancoli-Israel, Chesson, & Quan,

2007; Rechtschaffen & Kales, 1968). The first polysomnogram at 1 year post-injury (see Table 3, p. 21) was mildly abnormal with an overall sleep efficiency of 77.5% (time asleep divided by time in bed). Slow wave sleep (stages 3 & 4) was somewhat above normal limits at 35% (normal being approximately 20% of total sleep time) and total sleep time was 5.5 hours. REM sleep was mildly reduced at 16.3 % (normal is typically a quarter of the night).

The second polysomnogram at 3 years 8 months (see Table 3, p. 21) before the MWT revealed a sleep latency (time to enter sleep) of 22.5 minutes, which is typical of a sleep laboratory setting. Sleep efficiency was absolutely normal at 85%. Stage 1 sleep was increased at 10%, a marker of mild sleep disruption (typically, patients have 5% stage 1 sleep). Slow wave sleep (stages 3 and 4) was within normal limits at 26.2%. An adequate amount of REM sleep was seen at 23%. Most notably, a prolonged REM latency (172.5 minutes) was observed, likely due to citalopram; normally individuals reach REM sleep within the 90 minutes characteristic of the NREM/REM cycle. Periodic limb movements were noted (10 per hour is at the mildly increased level, with normal being less than 5 limb movements per hour) and limb movements may have interfered with sleep onset. No significant sleep disordered breathing was identified using a nasal pressure transducer (a few hypopneas is considered within normal limits in a patient of this age) and the lowest oxygen saturation was normal (92%).

The participant did not have a significant change in body mass index in this study and was 20.5 at the time of the second polysomnogram. A Maintenance of Wakefulness test followed the next day and the participant took his medications including modafinil on the day of the study. Despite the modafinil, the participant fell asleep in the first nap with a shorter than normal latency of 24.5 minutes for an average sleep latency of 36.1 minutes across all four assessments. Many sleep specialists consider a latency of 40 minutes to be normal on this test, and published normative values are available (Doghramji et al., 1997).

Table 13

Sleep Findings

	Sleep Study #1 (baseline)	Sleep Study #2 (follow-up)
Time post-injury	1 year	3 year, 8 months
Medications	Zopliclone	Lorazepam, Modafinil, Citalopram, Mirtazapine
Sleep Onset (min)	3.8	22.5
Total Sleep Time (H:MM)	5:15	7:20
Sleep Efficiency (%)	77.5	85.0
Stage 1 (%)	5.9	10.1
Stage 2 (%)	42.8	41.1
Stage 3 (%)	9.7	20.9
Stage 4 (%)	25.3	5.3
REM (%)	16.3	22.6
REM Latency (min)	136	172.5
Apneas	0	1 obstructive, 3 central
Hypopneas	0	10
Lowest Oxygen	95%	92%
Periodic Leg Movement Index (PLM Index)	4.9	9.8

3.7.2 Cognitive-Communication Findings

Compliance with completion of the DCCASP was 94% with only 6 days of missing data over the week of Christmas holidays. The DCCASP demonstrated a clear relationship between quality of sleep and language processing, sustained attention/vigilance, and memory across the different phases of the medication adjustment (see Figure 1) when modelled using an ARIMA(2,1,1) method. Sleep quality, attention functioning, memory functioning, language processing and mood (as measured by the DCCASP) changed over three distinct periods,

which mapped to the first, second through fourth, and finally the fifth medication adjustment. The median score for each of these subscales was 2.0 during the first medication regimen, and was elevated to, and remained constant at 3.0 for the second through fourth medication adjustments. During the final observation period the median score for each of the subscales was 4.0. Correspondingly, daytime sleepiness demonstrated the opposite relationship. Median scores during the first medication period were 4.0 and remained elevated until the final medication adjustment during which they decreased to a median of 1.5.

For each of the scales, time-series analysis demonstrated relative stability in scores when scores were averaged over 2 days (i.e., a 1-period lag function). Mood demonstrated the most variation, but a clear pattern associated with medication regimen appeared nonetheless. Qualitatively, these scores mapped well to clinical observations, as the participant was able to fully resume therapies and attend school such that he was able to successfully complete his remaining high school credits and graduate. Improvements in mood and an increase in socialization were noted by therapists and family members with reports of reduced irritability and perseveration, an increase in humour and increased engagement and social interactions. Improvements in subjective perception of function were clearly associated with the phasing-in of the treatment protocol overtime. Further, Spearman Rho analyses based on 108 observations in each domain, determined that perceived sleep quality (as measured by the DCCASP) was highly correlated with perceived daytime function, $p < 0.0001$ (sleep with memory, $r = 0.668^{**}$, sleep with attention, $r = 0.738^{**}$, sleep with language processing, $r = 0.683^{**}$ and sleep with mood, $r = 0.623^{**}$).

Each change in medication produced a positive change that built upon the previous positive change. In other words there was a building block approach to treatment culminating in outcomes that were subjectively identified as the best possible outcomes in each of the four cognitive-communication domains on the DCCASP.

A separate analysis using a standardized neuropsychological battery at 31 months indicated similar findings of improved neuro-cognitive functioning, especially on measures of verbal learning and memory, subtests of the Wechsler Memory Scale –III (WMS-III) and

the California Verbal learning Test-II (CVLT-II) (see Table 1, p. 7), and fewer mood symptoms on the Beck mood scales (BDI-II and BAI).

3.8 Discussion

To our knowledge, this study is one of the first of its kind to longitudinally document functional and self-reported improvements in cognitive abilities specifically related to or underlying communication (auditory attention, memory and speed of processing) and mood, and the first to examine communication abilities from the perspective of language processing in response to self–reported changes and improvements in sleep in an individual with severe traumatic brain injury. The clearly identified relationship between treatment of the sleep/wake and mood disorder, and the comprehensive and individualized approach to treatment may provide guidance to clinicians. Our results suggest that successful management of sleep/wake disturbances and mood post-traumatic brain injury, can potentially facilitate improvements in cognitive-communication function which may, in turn, facilitate participation in rehabilitation and community integration.

Further, the DCCASP profile was found to be clinically sensitive to clinical and self-reported observations of changes in cognitive-communication function (specifically, sustained auditory attention, language processing, and verbal memory) in relation to daytime arousal, as well as changes in mood, and indirect improvements in sleep quality. The participant found the measure to be particularly useful as it allowed him to see changes over time and heightened his self-awareness regarding the relationship between his sleep, wakefulness, mood and cognitive-communication abilities.

These findings suggest that evaluation and management of sleep and wake disturbances post-traumatic brain injury can potentially facilitate substantial improvements, as observed here through self-report, in cognitive-communication function in the areas of sustained attention/vigilance (to auditory verbal information), language processing and verbal memory, as well as in mood. All of these are important contributing factors to outcome and quality of life. It is important to note that we are not assuming a relationship of causality here. Rather, our findings suggest that by improving sleep and daytime wakefulness, we enabled the participant's potential for spontaneous recovery and response

to therapies. In addition, separate clinical neuropsychological evaluations demonstrated that the self-reported findings on the DCCASP closely mirror the results of a standardized, comprehensive neuropsychological battery.

While objective assessment of sleep and alertness are important, subjective perception of sleep and alertness may contribute significantly to the participant's experience. Parcell et al. (2006) highlight the importance of self-report, in that subjective reports of sleep quality and daytime functioning reflect each person's experience of sleep. They are of central importance to the diagnosis of sleep disorders and evaluation of treatments (Parcell et al., 2006). These findings support that the DCCASP may be a suitable tool to educate clients regarding the impact of their sleep patterns on daily cognitive-communication function, and can also be used to track subjective response to treatment of sleep and wake disturbances or changes in sleep and wake patterns. Thus, the DCCASP may provide additional guidance to clinicians in monitoring response to treatment over the long term.

From a clinical management perspective, this case is similar to the complex profile of many individuals with TBI who present with symptoms of disturbed sleep, reduced wakefulness and arousal concurrent with mood alterations. Further, consistent with other epidemiological reports of sleep and wake disturbances post-TBI, this individuals' impaired sleep/wake profile evolved over time, becoming most prevalent once he returned home and attempted a fairly taxing community re-integration program, including return to school in combination with therapy. A specific underlying aetiology of his difficulties is problematic to delineate. However, the clinical management suggests the contributions of a combination of issues: his mood, his sleep and his daytime arousal. The most clinically significant improvements were noted with the addition of alerting agents. The fact that he fell asleep during MWT despite having taken his regular dose of modafinil does suggest excessive daytime sleepiness, most likely due to underlying brain pathology secondary to the TBI.

Formal assessment of alertness is crucial, as higher cortical function depends critically on the ability to maintain attention and this can only happen optimally in an alert brain. Avoiding sedative medications such as benzodiazepines as a sleep aid is important as these

medications have significant adverse daytime effects on cognition. Cognitive behavioural therapies for sleep may be more appropriate where possible, and could be considered as a first line of treatment in the event that the participant has access to a professional with this type of training (Ouellet & Morin, 2006, 2007). Underlying sleep disorders must also be addressed prior to initiation of symptomatic therapies to ensure treatable conditions are not overlooked such as obstructive sleep apnoea.

3.8.1 Limitations and Methodological Issues

Although single case studies can provide valuable information on the impact of treatment and treatment efficacy, the results cannot be generalized to a larger population of individuals with TBI at this time. Further, as the study was observational and exploratory in nature, we did not administer any formal cognitive-communication or neuropsychological assessment measures immediately prior to the onset of treatment and following the stabilization of sleep and daytime alertness to elucidate functionally-reported changes. The subjective measure used here, DCCASP, is one that shows promise but is in the early stages of development. It is not possible to comment on its reliability and validity at this time but this will be explored in future studies. Finally, an MWT following the initial sleep assessment and polysomnography would also have been beneficial in formally identifying daytime arousal difficulties. The focus of treatment for sleep was largely pharmacological; we also recognize that there are potentially other forms of treatment such as cognitive behavioural therapies that have been shown to effective in the treatment sleep disorders after TBI (Ouellet & Morin, 2006, 2007).

3.9 Conclusions and Future Research Directions

This study longitudinally documented functional and self-reported improvements in cognitive abilities specifically related to/underlying communication and mood, and is the first to examine self-reported language processing and communication abilities in response to changes and improvements in sleep and wakefulness. This is important given that successful communication is inherently dependent on intact cognition. Further, the addition of the Daily Cognitive-Communication and Sleep Profile (DCCASP) has given us the

unique ability to track subtle daily changes in function in response to sleep and wakefulness, which might otherwise have gone, unnoticed.

Given the high prevalence of sleep/wake disturbances following TBI, coupled with the high prevalence of cognitive-communication impairments, it is important that sleep/alertness be routinely evaluated and monitored post-injury. Although the data presented are limited to 1 participant and are primarily through self-report, our findings suggest that appropriate, timely and effective diagnosis and management of sleep/wake disturbances post-TBI may facilitate improved self-reported cognitive-communication function. This may, in turn, facilitate self-reported participation in rehabilitation and community integration. There is a need for controlled studies with more participants to show the impact of treatment over time, perhaps involving a range of sleep interventions.

It is our hope that these findings may stimulate discussion regarding the need for systematic evaluation and treatment of sleep and wakefulness and their functional effects following traumatic brain injury.

Chapter 4
Evaluating the Impact of Treatment for Trauma Related Sleep and Wake Disorders on Recovery of Cognition and Communication in Adults with Chronic TBI

4. Abstract

Objective: To longitudinally examine the impact of post-traumatic sleep and wake disorders at baseline and after treatment to optimize sleep, on recovery of aspects of cognition, communication and mood in adults with chronic traumatic brain injury (TBI). **Hypothesis:** Proper assessment and treatment of sleep and wakefulness will facilitate optimal recovery and, result in clinically, statistically and functionally meaningful changes in aspects of cognition, and in communication and mood. **Design:** Prospective, longitudinal cohort outcome study. **Setting:** Community based. **Participants:** Ten adults with moderate-severe TBI and two adults with complicated mild TBI, age 18- 58, participated in the study. The sample included 6 males and 6 females and ranged from 1-22 years post-injury. **Interventions:** Individualized treatment for sleep/wake disorder. **Main Outcome Measures:** Insomnia Severity Index, Beck Depression and Anxiety Inventories, Latrobe Communication Questionnaire, Speed and Capacity of Language Processing, Test of Everyday Attention, Repeatable Battery for the Assessment of Neuropsychological Status, Daily Cognitive-communication and Sleep Profile. **Results:** Positive changes were observed for each measure, and across all subtests of all measures. Statistically significant changes were noted in the areas of insomnia severity, $p = 0.0005$, depression severity $p = 0.0044$, anxiety severity, $p = 0.014$, immediate memory, $p = 0.048$, auditory selective working memory, $p = 0.031$, language, $p = 0.002$, speed of language processing, $p = 0.001$. **Conclusions:** These results add to a small but growing body of evidence that sleep and wake disorders associated with TBI exacerbate trauma related cognitive, communication and mood impairments. As such, there is a clear need for the systematic evaluation and treatment of sleep and wakefulness.

Key words: sleep disorders, traumatic brain injury, communication, cognition

4.1 Introduction

Traumatic brain injury can result in both short and long-term physical, cognitive and neurobehavioural impairments for survivors. These impairments can result in devastating personal and societal consequences, impacting return to the community and pre-injury lifestyle (Wiseman-Hakes, MacDonald, & Keightley, 2010). Complaints of sleep disturbance, excessive daytime sleepiness and disorders of arousal have been well established as being among the most pervasive and common sequelae of traumatic brain injury (Wiseman-Hakes et al., 2009, 2011). Sleep/wake disturbances are prevalent across all levels of severity and across the continuum of recovery, often evolving over time. Up to 70% of survivors report symptoms of insomnia including difficulty falling asleep, staying asleep, sleep fragmentation and difficulties with early awakening (Parcell et al., 2006; Ouellet & Morin, 2006; Rao et al., 2008; Wiseman-Hakes et al., 2009). Studies involving polysomnography, an objective measure of sleep, report that 50% of those with moderate-severe TBI present with other treatable sleep disorders such as obstructive and central sleep apneas, restless leg, periodic leg movement disorder, post-traumatic hypersomnia and circadian rhythm shift disorder (Baumann et al., 2007; Castriotta & Murthy, 2011; Ouellet et al., 2006; Verma et al., 2007). Polysomnographic findings also report changes in sleep architecture amongst those with chronic TBI ($\geq$ 1 year), including decreased sleep efficiency (amount of time asleep divided by amount of time in bed) (Shekleton, Parcell, Redman, Ponsford, & Rjaratnam, 2010), increased percentage of stage 1 sleep (Ouellet & Morin, 2006), reduced percentage of both slow wave sleep (Parcell et al., 2008; Shekleton et al., 2010) and REM sleep (Parcell et al., 2008), as well as increased awakenings and arousals (Parcell et al., 2008).

Despite this however, the etiology of sleep and wake disorders remains poorly understood, and their impact on recovery, particularly, cognitive recovery, is only beginning to receive scientific attention (Mahmood et al., 2004; Wiseman-Hakes et al., 2011). Sleep-wake disturbances have been shown to further impact already-impaired cognitive and communication abilities post-TBI (Struchen et al., 2008; Wiseman-Hakes et al., 2011).

Individuals with cognitive, communication and sleep impairments often shy away from social and or work situations involving multiple conversation partners and or background noise. This is because they lack the attentional, executive and information processing resources to cope with the complex demands of communication in these environments (MacDonald & Wiseman-Hakes, 2010; Wiseman-Hakes et al., 2011). There is recent evidence indicating that sleep wake disorders exacerbate cognitive and communication impairments post-TBI. Bloomfield et al. (2010) concluded that individuals post-TBI with poor sleep quality (by self-report) demonstrated significantly poorer sustained attention than those with TBI who reported good quality of sleep. Sleep-wake disturbances are also associated with memory impairments that continue to be evident at least 3 months post-injury (Lundin, De Boussard, Edman, & Borg, 2006). Mahmood et al. (2004) demonstrated that sleep disturbance among patients with mild to severe TBI is associated with decreased executive functioning and speed of information processing. In addition, disruptions in cognitive processes such as attention, concentration, memory, reasoning, and language processing can affect communication processes, such as the ability to attend to and understand conversation (MacDonald & Wiseman-Hakes, 2010).

Yet despite the clearly defined association between post-traumatic sleep/wake disorders, and post-traumatic impairments in cognition and communication, studies examining interventions for sleep and wakefulness have not included measures of communication, and few have included measures of cognition as outcomes. In 2009, Wiseman-Hakes et al. completed a systematic review of the literature on sleep and wake disorders after TBI, addressing a number of sub-topics including intervention. Of the six intervention study papers reviewed, Ouellet and Morin (2004, 2007) included measures of mental health, Castriotta et al. (2009) included a measure of mental health and a measure of sustained motor performance, and Shan and Ashworth (2004) included the mini mental status exam as outcome measures. The rest focused primarily on sleep parameters, including total sleep time, sleep onset latency and number of awakenings. However, a recently published case study demonstrated that successful diagnosis and intervention to optimize sleep and wakefulness post severe TBI can optimize recovery of cognition and communication. In this case, long-term treatment of sleep and arousal beginning at 1 year post-injury resulted in

significant self-reported improvements in attention, memory, language processing and mood (Wiseman-Hakes et al., 2011). These gains were maintained over time and objective improvements were identified at 31 months post-injury in a follow-up neuropsychological examination

Therefore, although there is mounting awareness and evidence that sleep and wake disorders impede the recovery process and exacerbate other trauma related impairments, there has been limited research examining the impact of successful diagnosis and management of these disorders on outcomes for cognition and communication.

STUDY OBJECTIVE: To longitudinally examine outcomes for recovery of aspects of cognition, communication and mood in adults with chronic TBI and post-traumatic sleep and wake disorders. Outcomes were examined at baseline and after treatment to optimize sleep and or wakefulness. Additionally, we sought to examine any perceived change in participation outcome, in response to optimization of sleep and wakefulness.

HYPOTHESIS: Proper assessment and treatment to optimize sleep and wakefulness will facilitate optimal recovery outcomes for aspects of cognition, (speed of information processing, working memory, attention) communication (increased ability to participate in conversation, increased social communication) and mood and, result in clinically, statistically and functionally meaningful changes in cognition, communication and mood. We further hypothesize that optimization of sleep and or wakefulness will not result in changes to other aspects of cognition and communication such as visual spatial abilities, and vocabulary. Finally we hypothesize that optimization of sleep and wakefulness and optimization of cognition, communication and mood, will increase self-reported participation outcomes

4.2 Methods

The study was approved by the research ethics review board of the University of Toronto, Sunnybrook Health Sciences Centre, Toronto, University Health Network (UHN) Toronto Western Hospital, Toronto Rehabilitation Institute, and Bridgepoint Health Network West Park Hospital.

4.2.1 Participants

Participants were recruited from across Southern Ontario by means of clinicians working in major rehabilitation centres in Toronto, community based rehabilitation practitioners across Southern Ontario, and an announcement on the Brain Injury Association of Canada website. Clinicians were contacted by means of the professional association of speech language pathologists and audiologists of Ontario (OSLA), through research presentations, and through contact with physician program directors of the various trauma and rehabilitation centres across the Greater Toronto Area). Requests for information and participation were received from as far away as British Columbia; however, only 1 participant came from out of province. In order to be included in the study, participants had to meet the following criteria: (1) be between the ages of 18-60 years (2) have a diagnosis of moderate-severe traumatic brain injury or complicated mild traumatic brain injury as determined by one or more of the following: Glasgow Coma Scale Rating $\leq$ 12 (Teasdale & Jennett, 1974); post-traumatic amnesia $\geq$ 24 hours; retrograde amnesia; evidence of intracranial bleed; required neurosurgery; (3) be a minimum of 1 year post-injury in order to minimize the possible confound of spontaneous recovery; (4) have received documentation of cognitive-communication difficulties including challenges with attention, memory, information processing and social communication, either by professional, family member or self-report. (Social communication included things such as being able to participate in multi-speaker conversations, follow conversation in noisy environments and on the telephone, be able to respond quickly and appropriately in conversation); (5) have self-reported post-traumatic sleep and or wake disturbance (excessive daytime sleepiness), defined as dissatisfaction with sleep such that it was a cause of significant distress; (6) have obtained a score of 15 or greater on the Insomnia Severity Index,(Morin, 1993) (see Appendix P) during the initial interview. This represents “Clinical Insomnia” (see Measures) for those with night time sleep problems, and a score of 8-14 which represents “Sub-threshold Insomnia” for those with adequate or excessive night time sleep and excessive daytime sleepiness; (7) be functioning at a Level 8 or greater on the Rancho Los Amigos Cognitive Scale Revised (Malkmus & Stenderup, 1974), (Purposeful, Appropriate: Stand-by Assistance) such that they were able to cognitively

understand the purpose of the study and comply with the protocol as best they could; (8) be able to speak and read English; and (9) have provided written informed consent to participate. Individuals were excluded from the study if they (1) had a history of psychosis; (2) were actively using substances such as alcohol or nonprescription drugs; (3) had a pre-injury diagnosis of attention deficit disorder; or (4) had alcohol or caffeine the day and night before their polysomnography.

Table 14 provides demographic information on the 13 participants at baseline. Formal measures of participation were not administered; however, such factors as employment status, level of independence and socialization were noted and any changes in status were observed and recorded.

Table 14

Participant Demographics and Baseline Characteristics

ID #	Age	Sex	Glasgow Coma Scale	TBI Severity	Time Post Injury (years)	Marital Status	Education (years)	Participation Status	Body Mass Index	Co-morbid Depression	Insomnia Severity Index Score
1	18	F	3	Severe	2	Single	12	School with FT 1-1 Support; TBI rehab	25.4	Y	Severe
2	19	M	3	Severe	1	In relationship	14	School PT with support; TBI rehab	23.3	Y	Severe
3	21	M	N/A	Moderate-Severe	4.5	Single	12	Not Working	28.5	Y	Severe
4	28	F	3	Severe	2	Single	16	Not working; TBI rehab	25.2	Y	Severe
5	29	M	N/A	Severe	22	Married	14	Employed FT ; Working on GED	21.1	Y	Sub threshold
6	31	M	5	Severe	1	Married	16	Attempting RTW	21.3	Y	Moderate
7	32	M	N/A	Complicated mTBI	2	Single	18	Not working; PT student with support TBI rehab	22.1	Y	Moderate
8	37	F	N/A	Severe	2	Single	14	Not working; TBI Rehab	27.3	Y	Sub threshold
9	47	M	13	Complicated mTBI	2	Married	21	Working	32.8	Y	Severe
10	49	M	5	Severe	1	Divorced	10	Not working; TBI rehab	29.6	Y	Severe
11	53	F	5	Severe	3	Married	18	Not working	29.2	Y	Moderate
12	55	F	3	Severe	18	Married	16	Working	19.0	N	Moderate
13	58	F	N/A	Severe	1.5	Widowed	18	Not working	23.6	N	Moderate

Note: Depression determined by physician diagnosis

4.2.2 Study Protocol

Following receipt of the referral, an initial telephone contact was made to answer any questions, determine willingness to participate, and to set the first baseline data collection session if appropriate (see Telephone script, Appendix K). During the first session, the evaluation interview, participants signed the informed consent, and were administered the Insomnia Severity Index (Morin, 1993) and the Latrobe Communication Questionnaire (Douglas et al., 2007), the Beck Depression (Beck, Steer, & Garbin, 1988), and Anxiety (Beck, Epstein, Brown, & Steer, 1988) Inventories, participated in the Diagnostic Interview for Insomnia (Morin, 1993), and were provided instructions to begin regular completion of the Daily Cognitive-Communication and Sleep Profile (DCCASP) (Wiseman-Hakes et al., 2011) (see Measures). A list of other treating clinicians and baseline medications was obtained where applicable. A letter explaining their participation in the study was also sent to the family physician, and a referral for the sleep evaluation was requested, either from the referring physician (where applicable) or family doctor.

Session two involved a comprehensive clinical evaluation of sleep and wakefulness by a neurologist who was also a diplomate of the American Board of Sleep Medicine. At each clinical session, an Epworth Sleepiness Scale score was also obtained (Johns, 1991). Where indicated, participants were referred for blood work to evaluate endocrine function, ferritin levels, magnesium, and vitamin B12. This is because alterations in endocrine function—in particular, hypo-pituitarism or partial hypo-pituitarism—are reported in up to 68.5% of individuals at least 3 months post-TBI and these alterations can mimic sleep and cognitive difficulties (Bushnik, Englander, & Katznelson, 2007; Ghigo et al., 2005). Alterations in ferritin, magnesium and B12 can also contribute to difficulties with sleep and wakefulness. During session two, participants also underwent a baseline evaluation of neuropsychological status and cognitive-communication status, with the Repeatable Battery of Neuropsychological Status (RBANS) (Randolph, 1998), the Speed and Capacity of Language Processing (SCOLP) (Baddeley, Emslie, & Nimmo-Smith, 1992), and the Test of Everyday Attention (TEA) (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994). Scoring of the measures was conducted by a qualified research assistant (RA) who was blind to the status of the participants that the RA did not have any information regarding the

participants, and did not have knowledge as to whether the measures were pre- or post-intervention.

Session three involved overnight polysomnography and a Multiple Wake Test (MWT) (Doghramji et al., 1997) the following day where indicated. Once the polysomnography and daytime tests were reviewed and scored, participants returned for a follow-up appointment with the neurologist and sleep specialist to discuss findings, recommendations and treatment. All sleep assessments and intervention were conducted by the same physician and his sleep lab to ensure a standardized and comprehensive protocol. Treatment was prescribed on an individualized basis depending on the sleep diagnosis and the needs of the individual participant. Once treatment was initiated, participants continued to complete the DCCASP and report to the investigator on a weekly basis to determine progress, barriers and any issues impacting success of the treatment. Session four involved a follow-up appointment to discuss progress with the neurologist and sleep specialist. Once sleep and or wakefulness were optimized (as determined collaboratively with the neurologist and the participant), participants returned for a final follow-up assessment of neuropsychological status, mood, and cognitive-communication status. It should be noted that time to respond to treatment varied between participants, with the minimum time to respond to treatment(s) being 1 month, and the longest being over a year. Thus some required a number of follow-up appointments to optimize sleep and wakefulness. The average length of time that participants were followed throughout the study was 8 months.

4.2.3 Measures

4.2.3.1 Evaluation Interview

Diagnostic Interview for Insomnia (Morin, 1993) Appendix Q: This interview was designed to evaluate the presence of insomnia and determine possible contributing factors including: (a) Nature of the complaint; (b) Sleep-wake schedule; (c) Self report estimates of severity; (d) Impact on daytime function; (e) History and evolution of the complaint; (f) Environmental factors; (g) Medication use; (h) Sleep hygiene (e.g., caffeine use); (i) Presence of other sleep disorders such as apnea or periodic leg movements; (j) Medical

history; and (k) A Functional analysis to investigate antecedents, consequences, secondary gains, and precipitating and perpetuating factors. The interview is semistructured and takes approximately 45–60 minutes to complete.

4.2.3.2 Neuropsychological and Communication Battery

The test battery consisted of the following objective and self-report measures, chosen to meet the following criteria: to be repeatable; to assess those cognitive functions and mood states sensitive to sleep and sleep deprivation; to identify performance in the cognitive domains necessary for communication including auditory attention, information processing and working memory; and, to evaluate communication function.

1. *Test of Everyday Attention (TEA)* (Robertson et al., 1994): The TEA was designed to assess several independent attention systems in the human brain serving different functions in every-day behaviour. The TEA provides norm referenced scores on tests that are sensitive to selective attention, sustained attention, and attentional switching, as well as divided attention. This test was chosen in part because it is the only test of attention based largely on everyday materials; the real-life scenario means that patients enjoy the test and find it relevant to the problems faced in life, and has three parallel versions for test-retest purposes. Further, the primary mode of stimulus presentation is auditory, which underlies language processing and communication. Its psychometric properties have been well documented (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996).
2. *Repeatable Battery for the Assessment of Neuropsychological Performance (RBANS)* (Randolph, 1998)*:* The RBANS is one of the most commonly used measures of neuro/cognitive functioning in research, with well established and documented psychometric properties. It taps all major domains including language, immediate and delayed memory and attention. It provides standardized scores whereas many tests in this area are criterion cut off or provide just levels of severity. Another beneficial feature of the RBANS is its two parallel versions, which allows for test-retesting at any time (McKay, Casey, Wertheimer, & Fichtenberg, 2007). It is also one of the shorter batteries, which served to reduce the response burden of participants.

3. *Speed and Capacity of Language Processing (SCOLP)* (Baddeley et al., 1992)*:* This test is sensitive to the slowing of language and cognitive functioning that often occurs following brain injury. The SCOLP is composed of two brief tests, Speed of Comprehension Test and Spot-the-Word Vocabulary Test. The Speed of Comprehension Test allows the rate of information processing to be measured, and the Spot the Word Test provides a framework for interpreting the results of the first test. Four parallel versions of the Speed of Comprehension Test are available for test-re-test purposes. The psychometric properties of this test have been well established (Strauss, Sherman, & Spreen, 2006).

4. *Latrobe Communication Questionnaire (Latrobe QC)* (Douglas, Bracey, & Snow, 2000)*:* Appendix R: This self-report instrument measures perceived communication ability in a variety of domains including comprehension, expression, speed of processing and social comfort and communication competency, from self-perception. A reliable communication partner can also complete the measure. Content and test-retest reliability and discriminant validity have been demonstrated with adults following TBI. (Douglas et al., 2007)

5. *The Beck Depression Inventory–II (BDI–II)* is a 21-question multiple-choice self-report inventory that is one of the most widely used instruments for measu*ring the severity of depression over the past 2* weeks. The most current version of the questionnaire is designed for individuals aged 13 and over and is composed of items relating to depression symptoms such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex. It is widely used in clinical research and its psychometric properties have been well established (Beck, Steer, et al., 1988).

6. *Beck Anxiety Inventory (BAI):* This 21 item questionnaire is used to assess the severity of an individual's anxiety by evaluating the somatic and cognitive symptoms of anxiety over the last 7 days, and to discriminate between anxious and nonanxious diagnostic groups. The BAI has also been widely used in clinical research with well-documented psychometric properties (Beck, Epstein, et al., 1988).

7. *Daily Cognitive-communication and Sleep Profile (DCCASP):* Appendix S: The Daily Cognitive-Communication and Sleep Profile (DCCASP) is a series of seven self-report five-point Likert rating scales developed for use in clinical practice and as a research tool, as a means of monitoring daily fluctuations in cognitive-communication function in relation to quality of sleep. It was developed to fill a gap in available measures designed to evaluate sleep function by self-report, and the impact of sleep (or lack thereof) on daytime function. Its preliminary reliability and validity have been established in a normative population (Fung, Nguyen, Wiseman-Hakes, & Colantonio, 2011).

8. *Participation Measures:* These included employment status, participation in school (academic status), relationship status, participation in rehabilitation, level of independence and socialization. Note: Questions regarding employment, academic involvement, relationship status, particiption in rehabilitation were asked during the intitial interview and then informally throughout the study, and then formally again at the conclusion of the study. Levels of independence and socialization were informally determined through discussion with participants, their significant other and or rehab team where available. No formal measures of participation were used in the study, thus there are no participation measures included in the appendices.

4.2.3.3 Sleep Measures

1. *Polysomnography:* All polysomnograms were recorded on digital equipment (Compumedics Neuroscan, Australia) using standard recording and scoring methods (Iber et al., 2007). During each study, monitoring of the following took place: Electroencephalogram (EEG; electrodes C3, C4, O1, O2), A1, A2 (reference leads at the mastoids), electro-oculogram (EOG; LOC [below and lateral to left eye], ROC [above and lateral to right eye]), surface electromyography (EMG; mentalis/submentalis, anterior tibialis), respiratory measures (abdominal and thoracic effort [measured with respiratory inductive plethysmography belts], nasal/oral pressure [measured with a nasal/oral pressure transducer], nasal/oral flow [measured with a thermistor]), oxygen saturation, and a 2-lead ECG. Expanded EEG or EMG montages were used if nocturnal

seizures or parasomnias were suspected. All studies were videotaped and audiovisual recordings were time-synchronized to the remainder of the data. Sleep was manually scored according to the American Academy of Sleep Medicine [AASM] criteria (2007). Multiple Sleep Latency Tests (MSLT) or Multiple Wake Tests (MWT) were obtained using conventional criteria suggested by the AASM. All studies had been interpreted by a diplomate of the American Board of Sleep Medicine and scored by a registered polysomnographic technologist. Sleep disorder diagnoses were made after clinical assessment according to the International Classification of Sleep Disorders (ICDS-2) (AASM, 2005). The purpose of the polysomnogram was to determine the following measures:

- Sleep efficiency: time asleep / time in bed (measured in percent)
- Total sleep time
- Total number of awakenings
- Total arousal index (number of arousals but not fulll awakenings per hour)
- Apnea/hypopnea Index: The number of obstructive events (complete or nearly complete obstruction of airflow) combined with the number of obstructive hypopnea events (a partial reduction in airflow, of > 30% of baseline with preservation of respiratory effort) per hour.
- Lowest level of oxygen saturation (O^2 sat) measured in percentage
- Periodic leg movements (measured per hour)
- Percentage of time spent in sleep stages 1, 2, and 3
- Percentage of time spent in REM sleep

2. *Maintenance of Wakefulness Test (MWT)* (Doghramji et al., 1997): This involves giving the participant four opportunities to maintain wakefulness during the day at 9 a.m., 11 a.m., 1 p.m., 3 p.m., for 40 minutes each time. They are placed in a slightly reclined position , in a dimly lit room, with the instructions “Please sit quietly and try to remain awake”. Participants are not woken if they fall asleep. For this study, we interpreted 1 epoch (instance) of sleep to be a fail. The MWT has also been confirmed as an important

test to identify EDS, as well as to provide an indicator of future risk of accidents (Doghramji et al., 1997; Coelho, Narayansingh, & Murray, 2011).

3. *Epworth Sleepiness Scale (ESS)* (Johns, 1991): This 5 question scale was designed to evaluate daytime sleepiness, and asks the respondent the likelihood that they would fall asleep under various scenarios. This questionnaire was administered as part of the routine clinical evaluation of sleep. A normal score is 4.6 with a range of 0-10. The reliability and validity of the ESS has been well established (Johns, 1992).

These sleep measures were abstracted from clinical records (see Appendix T).

4.2.4 Analysis

Data were analyzed in two formats: as a single case series, including descriptive information, and as aggregate data. The assessment of results obtained from objective measures and self-report questionnaires was made through statistical analysis using paired nonparametric Wilcoxon Signed Rank tests on the SAS 9.2 (SAS Institute Inc., 2008) and were used to examine group changes in scores at entry into the study and upon optimization of sleep and wakefulness (i.e., pre–post measures). The Wilcoxon Signed Rank test was chosen due to the small sample size and high variation both at baseline and at follow-up among the sample (i.e., no normal distribution of the sample). In order to take a conservative approach to the analysis, a Bonferroni correction was then applied 'to correct for the large number of measures' in our protocol, and thus control for the possibility of Type 1 errors. To calculate the DCCASP results, we took the average rating score for the week for each variable and plotted these over time in order to visualize any trends and or response to intervention.

4.3 Results

Twenty-one individuals with TBI were referred for this study. Of these, one began the study and then withdrew after the initial evaluation due to the distance required to travel for the polysomnography and medical appointments, which were held at Sunnybrook Health Sciences Centre in Toronto. Seven individuals either did not meet the inclusion criteria because they either lived outside of the province of Ontario (thus were unable to provide

necessary funding for travel and accommodation), or were no longer interested in participating following the initial telephone screening. Only one person was formally excluded since his brain injury was a result of a tumour that was subsequently removed, so it did not fall under the category of traumatic. In total, 13 individuals enrolled in the study, and one was lost to follow-up after the sleep and baseline neuropsychological and communication data were obtained. Twelve participants completed the study.

Eleven individuals with moderate-severe TBI and two with complicated mTBI participated in this study. Refer to Table 14 for socio-demographic information and clinical characteristics from the medical records. The mean age of participants was 36.9 years (median 28 years, SD: 14.1; range 18-58 years) and the mean years of education were 15.3 (median 25.8 years, SD; 3.04; range 10-21 years). There were 6 females and 7 males; 5 were married, 1 was widowed, 1 was divorced, 1 was in a relationship and 5 were single. The mean time post-injury was 4.8 years (median 15.3 years, SD: 6.9; range 1-22 years).

4.3.1 Participation

At the onset of the study, 3 participants were in school, 1 with full-time 1-1 support, and 2 with partial support. Six were not working (unable to work), 2 were working in paid employment, 1 was working in a volunteer capacity and 1 was attempting a graduated return to work. Six were still in active rehabilitation. All reported reduced socialization in comparison to pre-injury levels, due to fatigue, and cognitive-communication difficulties. Eleven participants reported being uncomfortable and or lacking confidence in situations requiring social communication. Seven reported reduced levels of independence at baseline, and one individual's spouse was very actively involved, almost assuming a role of therapist. Upon completion of the study, 1 of the participants previously not working returned to work part-time, one began to pursue return to work, and one of the students attending school part-time (pursuing an online college degree) was able to increase their course-load. One of the younger participants, who had been living at home with their family, was able to move in to a partially supervised independent living situation (a group home). The participant whose spouse had been so actively involved reported that they were able to 'pull back' somewhat and return to more of a partner role. It is possible that

for the six involved in active rehabilitation at the time of the study, their participation in rehabilitation may have played a role in their increased participation. However, all reported that they perceived their increase as being a result of improved sleep and wakefulness.

4.3.2 Sleep

All 13 participants had a (relatively) treatable sleep and/or wake disorder. While we recruited on this basis, this finding, in and of itself, was important given that 2 of the participants were more than 15 years post-injury, and both had been struggling with trauma-related sleep disorders that had previously never been addressed. Further, 1 participant who was 2 years post-injury, had undergone PSG at another centre, however she was told that essentially nothing could be done, and was not offered any intervention. Two participants who were actively driving at the onset of the study, failed their MWT's and subsequently had their drivers licenses revoked until they were adequately treated and could pass a follow-up MWT.

The International Classification of Sleep Disorders (ICSD-2) (AASM 2005), lists 84 sleep disorders under 8 major categories, including: (1) insomnias; (2) sleep-related breathing disorders; (3) hypersomnia not due to breathing disorders, (4) circadian rhythm sleep disorders; (5) parasomnias; (6) sleep-related movement disorders; (7) other sleep disorders; and (8) isolated symptoms, apparently due to adverse effect of drugs, medications and biological substances.

All 13 TBI participants underwent baseline sleep studies. Polysomnography (PSG) data from these studies are reported in Tables 15 and 16. After analysis of PSG and MWT data, 3 of the 13 participants (23%) were diagnosed by a licensed sleep specialist with hypersomnia according to the ICSD-2 (2005) criteria. Three (23%) were diagnosed with sleep-related breathing disorders (SRBD), of which two (15%) had obstructive sleep apnea (OSA) and 1 (8%) had both OSA and central sleep apnea (CSA), 4 participants (31%) were diagnosed with insomnia/EDS, 1 (8%) with periodic limb movements in sleep (PLMS) and 1 (8%) had circadian rhythm disturbance (CRSD) combined with PLMS. One participant (8%) was diagnosed with both EDS and restless leg syndrome (RLS). For the purpose of

this analysis, this participant was grouped with the Insomnia/EDS participants, since these were his primary diagnoses. The participant with CRSD and PLM was placed in the PLM group. Participants diagnosed with SRBD (two with OSA and one with OSA and CSA) had a mean apnea-hypopnea index (AHI) of 35.3. Two of these participants had impaired alertness based on MWT. Those diagnosed with PLMS had a mean PLM index of 23.9 and mean arousals index of 15.2. These participants had objectively well-maintained alertness (as per their MWT results).

Table 15

Polysomnography and Sleep Findings A

Sex	ID#	Sleep Diag-nosis	Sleep Latency (mins) Time to fall asleep	Age Norm	Wake After Sleep Onset (mins)	Sleep Efficiency in %	Age Norm (%)	Total Sleep Time (hr:min)	Total Awaken-ings	Total Arousal Index (Norm: <10/hr)	Apnea Hyponea Index (Norm: <5/hr)	Lowest o2 Sat in % (Norm: 90-100%)	Periodic Leg Mvmt/hr (Norm: <5/hr)
F	1	HS	10.5	<20	12.5	95.	90-100	7:37	12	3	0.2	95	0
F	4	Insom & EDS	106*	<30	88.5	50.8*	85-95	3:21	4	6.9	0	93	2.4
F	8	CRSD & PLM	73.5*	<30	63	65.5 *	85-95	4:20	15	14.3*	0	93	16.6*
F	11	Insom & EDS	3	<30	36	90	85-95	6:29	28	6.2	11.1*	88*	0
F	12	OSA	27	<30	127.5	60.5*	85-95	3:57	24	24.1*	22.5**	88 *	0
F	13	OSA	28.5	<30	114	70.3*	85-95	5:39	29	27.3*	53.1**	79*	0
M	2	Insom, EDS & RLS	28.5*	<20	18.5	88*	90-100	6:30	20	8.7	0.2	93	0
M	3	Insom & EDS	53*	<30	121.0	61.5*	85-95	4:54	20	7.3	0	91	1.4
M	5	Insom & EDS	12.5	<30	35	87.3	85-95	5:29	12	11.7*	1.1	90	11.8*
M	6	HS	14.5	<30	30	91.6	85-95	8:25	21	6.6	0.1	92	2.7
M	7	HS	63*	<30	58	73*	85-95	5:26	35	11*	3.9	92	3.3
M	9	OSA, CSA, Insom & EDS	3	<30	59	88.2	85-95	7:42	17	9.6	30.3*	78*	0
M	10	PLM	46.5*	<30	198	53.4*	85-95	4h40m	47	16.0*	0	91	31.2**

All the insomnia/EDS group participants who completed the Epworth Sleepiness Scale (ESS) (4 out of 5) were sleepy by self-report with a mean ESS score of 13.25. Two of 5 participants underwent MWT and had abnormal MWT findings, suggesting an inability to maintain alertness throughout the day. Of the 3 participants with SRBD, 2 (66.7%) had abnormal MWT findings. Of the 3 with relatively "normal" (i.e., considered as mildly abnormal) polysomnographic data, 2 were unable to maintain alertness as per MWT and one had MWT findings considered normal—however this person was taking Ritalin at the time of assessment. (Note: a washout of Ritalin was attempted by this participant prior to his PSG and MWT, however, he was unable to function without it. Other participants did not take any prescribed stimulants the day of the MWT)

While the sleep diagnoses varied, all participants had a diagnosis of traumatic brain injury, 10 in the moderate-severe category, and two in the complicated mild category (i.e., they continued to present with unresolved symptoms of brain injury). When we consider the sleep findings from the perspective of TBI, we see a number of trends, including reduced total sleep time, reduced sleep efficiency and increased sleep onset latency (see Table 15, p. 99). Further, each participant exhibited abnormal sleep architecture, both due to sleep fragmentation as well as alterations in sleep staging, including increased stage 1 sleep, reduced slow wave sleep, and alterations in REM percentage and or REM onset latency (see Table 16). These findings may be due to abnormal events occurring during sleep, and possibly to effects of medication. When sleep was considered according to individual sleep diagnosis, we identified that the group with sleep disordered breathing and PLMS displayed greater amounts of lighter stages of sleep of (i.e., stage 1), indicating the impact of sleep fragmentation, which was also greater in these two groups. This is not surprising given their self- and significant-other reports of impaired daytime function. Stage 2 sleep was well maintained across all participants. The amount of deep sleep (i.e., delta sleep stage 3 and 4) has shown a different distribution across the group as a whole, with the greatest reduction seen in the sleep disordered breathing group as expected. REM sleep has been significantly delayed in all groups with the exception of the sleep disordered breathing group.

Table 16

Polysomnography and Sleep Findings B

Sex	ID#	Meds at PSG (baseline)	Med effect on sleep	Sleep Diag-nosis	Total Sleep Time (hr: min)	Stage 1 %age	Age Norm	REM %age	Age Norm	REM latency Norm: 90-120	Stage 2 %age	Age Norm	Stage 3 % age	Age Norm	ESS Or MWT Abnor-mal = *
F	1	Quetiapine	Y	HS	7:37	3.0	3.74	20	22.12	29.5 * reduced	50	49.43	27 *ample	23.43	I MWT* Latency 8.13
F	4	Teva-Trazedone Zopiclone Apo-Sertraline Apo-Doxycycline Ratio-Lenoltec	Y	Insom & EDS	3:21	4.5 * reduced due to limited total sleep time	4.18	10.7* reduced	25.23	87.5 mildly reduced	43 *	52.37	41.8* 'ample'	17.69	Epworth 16* MWT not done
F	8	Synthroid Plavix Cipralex Docusate sodium Apo-Atorvastatin Teva-Pranol	Y	CRSD & PLM	4:20	16.3* >	4.17	Absent ***	26.22	Prolonged*	57 *	53.77	26.7 * 'ample'	14.0	Normal MWT
F	11	Lamotrigine	Minimal	Insom & EDS	6:29	7.3* mild >	4.85	21.8	21.77	117.0	51 *	57.80	19.9*	10.63	Epworth 15* MWT latency 14.4*
F	12	None	NA	OSA	3:57	25.3* >>	4.85	20	21.77	66.0* reduced	49.6*	57.80	5.1** very reduced	10.83	Epworth 2
F	13	Metoprolol Amiodarone Foxetine Calcium Vit D Atrovastin Eltroxin Warfarin	Y	OSA	5:39	30.4* >>	4.85	29.1* increased	21.77	70.0 mildly reduced	40.1*	57.80	0.4** decreased	10.63	MWT Latency 26*
M	2	None	NA	Insom , EDS & RLS	6:30	9.2%* >	3.74	19.1	22.01	128.5 * mildly increased	52.4*	49.05	19.3*	23.04	Epworth 7 MWT missing
M	3	Cipralex	Y	Insom & EDS	4:54	19.7* >>	4.18	23.8	28.00	252.2** prolonged	36.8*	45.54	19.7*	21.09	MWT* Latency 18.3
M	5	Wellbutrin Risperidone Pristiq	Y	Insom & EDS	5:29	10.3* >	41.7	5.6** reduced	23.47	251.0 ** prolonged	71.2* >	56.89	12.9 * decreased	12.46	MWT missing Epworth 15*

Sex	ID#	Meds at PSG (baseline)	Med effect on sleep	Sleep Diag-nosis	Total Sleep Time (hr: min)	Stage 1 %age	Age Norm	REM %age	Age Norm	REM latency Norm: 90-120	Stage 2 %age	Age Norm	Stage 3 % age	Age Norm	ESS Or MWT Abnor-mal = *
M	6	None	NA	HS	8:25	9.9* >	4,17	27.6* increased	23.47	83 mildly reduced	58.9*	56.89	3.7**** very reduced	12.46	MWT Latency 23.8*
M	7	Modafinil Wellbutrin Cipralex	Y	HS	5:26	10.0* >	4.17	10.7* reduced	23.47	286* prolonged	58.2*	56.89	21.1* decreased	12.46	Epworth 14* MWT normal ON Modafinil
M	9	Mylan-topiramate PMS-methlyphenidate Cymbalta Co-meloxicam Ralivia Lyrica Butran patch	Y	OSA,CSA , Insom & EDS	7:42	11.0* >	5.64	10.1* reduced	22.85	121.0* mildly increased	59.7*	54.75	19.2*	8.85	MWT latency 8.1*
M	10	Citalopram Nortriptyline Amplodipine Metroprolol	Y	PLM	4:40	33.2** >>	5.64	12.1* reduced	22.85	119.5 ** prolonged	50.8*	54.75	3.9***** very decreased	8.85	Normal MWT but Epworth 14*

Note. MWT * indicates participant fell asleep (should be able to maintain wakefulness across 4 trials)
Epworth * indicates score > 10

Those who had components of insomnia as part of, or as their primary diagnosis, were more 'complex' and more difficult to treat, and thus the level of objectively measured and self-reported improvements in cognition and mood were somewhat less than for those participants with a 'less complex', or more objectively treatable' diagnosis such as apnea or RLS.

Table 17

Statistical Analysis of Pre-Post Measures Group Data

Test	Median		Lower Quartile		Upper Quartile		Range		P value	Corrected P value
Insomnia Severity Index (R)	T1	17.0	T1	17.0	T1	22.0	T1	10–26.0	0.0005*	0.0003*
	T2	8.5	T2	2.5	T2	13.5	T2	2.0–21.0		
Insomnia Severity Index (S)	T1	3.0	T1	3.0	T1	4.0	T1	2.0–4.0	0.0020*	0.0140*
	T2	2.0	T2	1.0	T2	2.0	T2	1.0–4.0		
Beck Anxiety Inventory (R)	T1	15.0	T1	10.0	T1	20.0	T1	6.0–26.0	0.0142*	0.0990
	T2	5.0	T2	2.5	T2	11.0	T2	0.0–20.0		
Beck Anxiety Inventory (S)	T1	2.0	T1	1.0	T1	3.0	T1	1.0–4.0	0.1563	1.0
	T2	1.0	T2	1.0	T2	2.0	T2	1.0–3.0		
Beck Depression Inventory (R)	T1	26.0	T1	19.0	T1	28.0	T1	11.0–32.0	0.0044*	0.0310*
	T2	15.0	T2	8.5	T2	19.0	T2	8.5–19.0		
Beck Depression Inventory (S)	T1	3.0	T1	2.0	T1	3.0	T1	1.0–4.0	0.0781	0.5470
	T2	2.0	T2	1.0	T2	2.5	T2	1.0–4.0		
Latrobe CQ	T1	63.0	T1	52.0	T1	70.0	T1	43.0–70.0	0.1475	1.0
	T2	55.5	T2	46.5	T2	60.0	T2	46.5–60.0		
RBANS Attention	T1	72.0	T1	68.0	T1	94.0	T1	64.0–132.0	0.0996	0.6930
	T2	91.0	T2	85.0	T2	116.5	T2	60.0–118.0		
RBANS Immediate Memory	T1	81.0	T1	76.0	T1	97.0	T1	61.0–123.0	0.0480*	0.3360
	T2	101.5	T2	76.0	T2	112.0	T2	61.0–112.0		
RBANS Delayed Memory	T1	83.0	T1	60.0	T1	94.0	T1	48.0–98.0	0.0500*	0.3710
	T2	94.0	T2	77.0	T2	99.0	T2	44.0–112.0		
RBANS Visual Spatial (*min change expected in response to > sleep)	T1	72.0	T1	69.0	T1	78.0	T1	60.0–84.0	0.1621	1.0
	T2	79.5	T2	78.0	T2	87.0	T2	64.0–96.0		

Test	Median		Lower Quartile		Upper Quartile		Range		P value	Corrected P Value
RBANS Language	T1	84.0	T1	78.0	T1	90.0	T1	47.0–100.0	0.0020*	0.0140*
	T2	99.0	T2	93.0	T2	101.0	T2	85.0–108.0		
RBANS Total Score	T1	71.0	T1	65.0	T1	85.0	T1	62.0–104.0	0.0020**	0.0140*
	T2	92.5	T2	74.5	T2	103.0	T2	62.0–109.0		
RBANS Percentile Score	T1	2.0	T1	1.0	T1	16.02	T1	1.0–61.0	0.0020**	0.0140*
	T2	31.0	T2	4.5	T2	58.0	T2	1.0–73.0		
SCOLP Speed	T1	10.0	T1	5.0	T1	48.0	T1	1.0–48.0	0.0010**	0.0070*
	T2	73.5	T2	55.0	T2	81.5	T2	28.0–99.0		
SCOLP Word (*min change expected in response to > sleep)	T1	25.0	T1	20.0	T1	50.0	T1	1–95.0	0.8860	1.0
	T2	25.0	T2	15.0	T2	42.5	T2	3.0–93.0		
TEA aud sel working mem	T1	15.0	T1	7.0	T1	75.0	T1	1.0–75.0	0.0310*	0.2170
	T2	50.5	T2	44.0	T2	75.0	T2	1.0–75.0		
TEA aud sel verbal mem	T1	10.0	T1	5.0	T1	36.0	T1	4.0–99.0	0.1680	1.0
	T2	46.0	T2	14.0	T2	75.0	T2	2.0–90.0		
TEA div attn working mem	T1	5.0	T1	1.0	T1	25.0	T1	1.0–99.0	0.1150	0.8050
	T2	42.5	T2	25.0	T2	78.5	T2	3.0–99.0		
TEA sel visual attention	T1	6.0	T1	2.0	T1	42.0	T1	1.0–82.0	0.0630	0.4410
	T2	10.0	T2	5.0	T2	43.0	T2	1.0–99.0		
TEA sel visual Attn (1 min)	T1	13.0	T1	5.0	T1	63.0	T1	1.0–84.0	0.0300*	0.2100
	T2	61.0	T2	30.0	T2	75.0	T2	2.0–92.0		
TEA sel visual Attn (2 min)	T1	7.0	T1	2.0	T1	63.0	T1	1.0–84.0	0.0440*	0.3080
	T2	40.0	T2	7.0	T2	75.0	T2	2.0–92.0		
TEA sus aud attention(severity level) lower = better	T1	1.0	T1	1.0	T1	3.0	T1	1.0–3.0	0.1250	0.8750
	T2	1.0	T2	1.0	T2	1.0	T2	1.0–2.0		

Test	Median		Lower Quartile		Upper Quartile		Range		P value	Corrected P Value
TEA sus aud vigilance	T1	10.0	T1	10.0	T1	25.0	T1	1.0–75.0	0.1270	0.8890
	T2	50.0	T2	25.0	T2	75.0	T2	25.0–75.0		
TEA vis attn. switching accuracy	T1	50.0	T1	25.0	T1	75.0	T1	5.0–75.0	0.5000	1.0
	T2	75.0	T2	48.0	T2	75.0	T2	5.0–75.0		
TEA vis attn. Switching speed	T1	4.0	T1	1.0	T1	22.0	T1	1.0–99.0	0.3950	1.0
	T2	22.5	T2	1.0	T2	60.0	T2	1.0–99.0		

Note. Wilcoxon Signed Rank Test and Wilcoxon with Bonferroni Correction; R = Raw Score; S = Severity Score.

With respect to aggregate data, positive changes were noted on each sub-test of every measure administered, after response to treatment of sleep and or wakefulness, as shown in Table 17. The greatest effect size however, was observed in the areas of speed of information processing (SCOLP Speed of Comprehension subtest, (corrected p = 0.007), language (RBANS language) (corrected p = 0.014), as well as the RBANS total test score, including which includes attention and memory subtests (corrected p = 0.014) and mood (Beck Depression Inventory, corrected p = 0.031), as shown in Table 17. These findings are consistent with our hypothesis that those cognitive domains underlying successful communication, that is, sustained auditory attention and speed of information processing, would be most sensitive to changes (in this case improvements) in sleep. Further, mood is highly sensitive to sleep restriction (Yoo et al., 2007) and so we anticipated that mood would improve with improvements in quantity and quality of sleep, and or improvements in quality of wakefulness and arousal. We expected to see improvements in social communication as measured by the Latrobe QC; although we did see improvements in scores (and reported functional improvements), the magnitude of change was not statistically significant. Our findings also support our hypothesis that we expected to see little or no change in vocabulary in visual spatial function and visual spatial attention, and the range of scores remained the same for these subtests.

When we examine the data on an individual basis, we see that 2 of the participants (participant #6 and #9) had extremely high objectively measured neuropsychological

scores at baseline, and for these two individuals, it is possible that this battery was not sensitive enough to pick up their subtle, yet highly debilitating impairments. However, their perception of sleep and function as measured by the DCCASP (see Figure 8, participant #6 & #9) does capture the impact of these impairments and their response to intervention.

When we consider the results, it is important to note that participants were very different in their presentations at baseline and throughout the study, which was not unexpected, given the heterogeneity typically seen with the diagnosis of TBI. While they all shared a diagnosis of either moderate-severe TBI, or complicated mTBI, and all had—and were aware of—cognitive and communication impairments, some were very adept at compensating. As such, these individuals were quite high functioning at baseline. Further, one individual with diagnoses of both obstructive and central sleep apnea and insomnia (participant #9) responded to treatment of his apnea, but continued to present with very significant insomnia. He reported that his sleep improved slightly over the course of the study, but he continued to struggle due the insomnia and external pressures of attempting to maintain employment status and family responsibilities. By the end of the study, although not the end of his clinical treatment of sleep, many of his objective and self-report scores worsened. While this may have reduced the magnitude of change and statistical significance of our findings, this finding does in fact, support our hypothesis, as this individual continued to present with sleep impairments, which further exacerbated cognitive, communication and mood impairments.

Questionnaires: At post-treatment, all 12 participants rated their sleep as being improved (in varying degrees) on the Insomnia Severity Index, and 10 of 12 reported improvements in their overall level of insomnia severity. All 12 participants reported improvements in mood raw scores; however, one individual remained in the severe category of depression as measured by the BDI. Measures of anxiety also improved for 10 of 12 participants, and 2 participants reported an increase in anxiety, which they reported as being due to pressures of, or changes in employment status. In regards to communication, 8 of 12 reported improved perception of their overall communication competence, as measured by the

Latrobe QC, 2 of 12 perceived their overall communication competence as being the same, and 2 of 12 perceived their communication competence as being somewhat worse. All continued to report that they found group conversations difficult to follow. However, whereas they tended to avoid this type of social interaction whenever possible at baseline, 11 of 12 reported somewhat of an increase in comfort in this situation at follow-up.

Objective Measures: When individual participant scores are examined, we see that 11 of 12 participants displayed a statistically significant improvement in speed and capacity of language processing as measured by the SCOLP subtest 'speed'. On subtests of the RBANS, 7 of 12 participants showed improvements in their immediate memory, and 10 of 12 showed improvements in their delayed memory scores. Two remained the same for immediate memory, and 3 showed a modest decrease in scores. One remained the same for delayed memory and one showed a modest decrease in score. Ten of 12 participants showed improvements in language, driven primarily by improvements in semantic fluency, (which is a reflection of processing speed) and 2 of 10 remained the same. Eight of 12 showed improvements in attention, 2 remained the same, and 2 showed a modest decrease in scores. As previously stated, we were not expecting to see much change in visual spatial ability, nor is it directly related to communication (with the exception of facial recognition and perception of emotion) so it was not an area of particular interest. However, 5 of 12 participants showed improvements in scores, 4 of 12 remained the same, and 3 of 12 showed a modest decrease. On overall RBANS raw scores and percentile scores, 10 of 12 participants showed improvements, and 2 remained the same.

The TEA was where we saw the most variability of performance and subsequent scores. Some of the subtests are quite difficult, and it was on this test that we saw the greatest impact of fatigue. As we were interested in the impact of attention as it pertains to communication, we anticipated the greatest improvements in auditory verbal working memory (subtests *elevator counting with distraction, and elevator counting with reversal)* and sustained auditory attention/vigilance (subtest *lottery).*in response to improvements in sleep. For these subtests, 7 of 12 participants improved their auditory verbal working memory scores, 2 remained the same, and 3 showed decreases in performance and scores.

Nine of 12 showed large improvements in sustained auditory attention, 1 remained the same, and 2 showed a decrease in scores in comparison to pre-treatment levels.

Ten participants completed the DCCASP. Although we have basline data and sleep data for participant #3, this individual was loss to follow-up as he developed psychosis, and was subsequently referred (by the research team) for appropriate treatment to psychiatry, physiatry and then to a community based rehabilitation program. Participant's number 6 and 8 did not complete the DCCASP due to the daily response burden. (Note we did attempt tp provide support t faciltate completion but were not successful). All participants who completed the DCCASP reported self-perceived changes in cognitive function (attention, memory) and communication (language processing) in response to optimization of sleep (see Figure 8, pp. 114-133). For those who required different treatments, there was a clearly observed improvement in function when treatment was optimized. The DCCASP was particularly helpful in determining when an individual did not respond to the intervention prescribed, and so needed to be re-evaluated Further, all participants reported that completion of the DCCASP facilitated their awareness of their sleep and their understanding of its direct relationship with their daytime cognitive and communication function, their mood and their level of fatigue.

Table 18

Mood and Sleep Raw Scores

ID #	BDI baseline	BDI post	BAI baseline	BAI post	ISI baseline	ISI post
1	28 (moderate)	9 (minimal)	20 (moderate)	6 (minimal)	17 (moderate)	2 (no clinical sig)
2	26 (moderate)	21 (moderate)	25 (moderate)	10 (mild)	22 (moderate)	9 (subthreshold)
3	23 (moderate)	16 (mild)	6 (minimal)	10 (mild)	26 (severe)	13 (subthreshold)
4	26 (moderate)	18 (mild)	16 (moderate)	20 (moderate)	14 (subthreshold)	3 (no clinical sig)
5	29 (severe)	15 (mild)	15 (mild)	1 (minimal)	17 (moderate)	14 (subthreshold)
6	19 (mild)	7 (minimal)	15 (mild)	4 (minimal)	21 (moderate)	9 (subthreshold)
7	30 (severe)	15 (mild)	10 (mild)	13 (mild)	13 (subthreshold)	8 (subthreshold)
8	28 (moderate)	34 (severe)	14 (mild)	12	22 (moderate)	21 (moderate)
9	19 (mild)	14 (mild)	21 (moderate)	1 (minimal)	25 (severe)	2 (no clinical sig)
10	24 (moderate)	20 (moderate)	9 (mild)	4 (minimal)	23 (severe)	20 (moderate)
11	11 (minimal)	1 (minimal)	7 (minimal)	0 (none)	17 (moderate)	2 (no clinical sig)
13	13 (minimal)	8 (minimal)	12 (mild)	5 (minimal)	10 (subthreshold)	7 (no clinical sig)

Note. BDI: 6 improved classification; 5 remained same classification with improved raw scores; 1 became worse
BAI: 8 improved classification; 3 remained same classification but 2 had raw scores improve 1 had raw scores worsen, 1 worsened classification;
ISI: 10 improved classification; 2 remained same classification but raw scores improved; 1 remained same

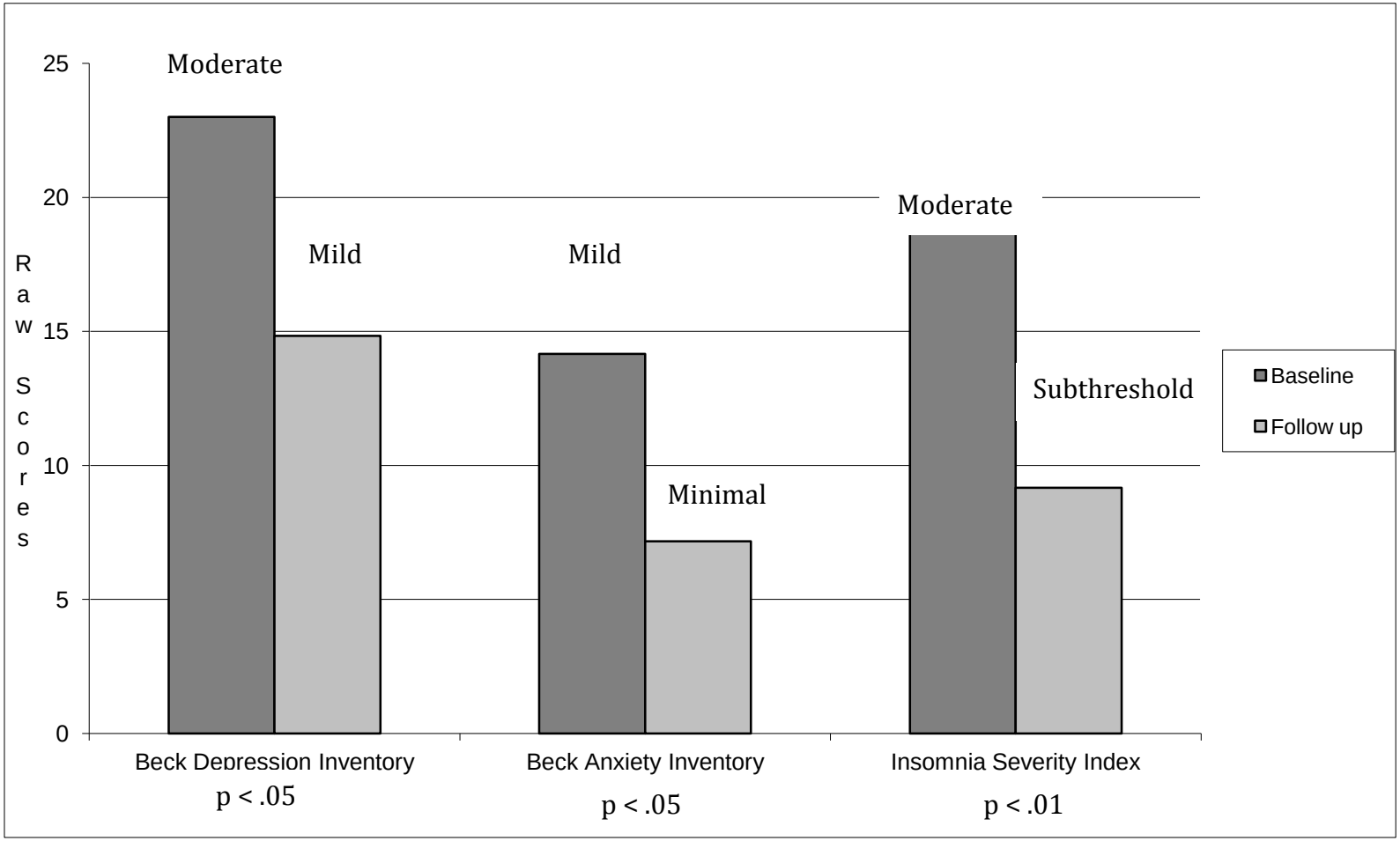


Figure 4. **Results for sleep and mood (N = 12).**

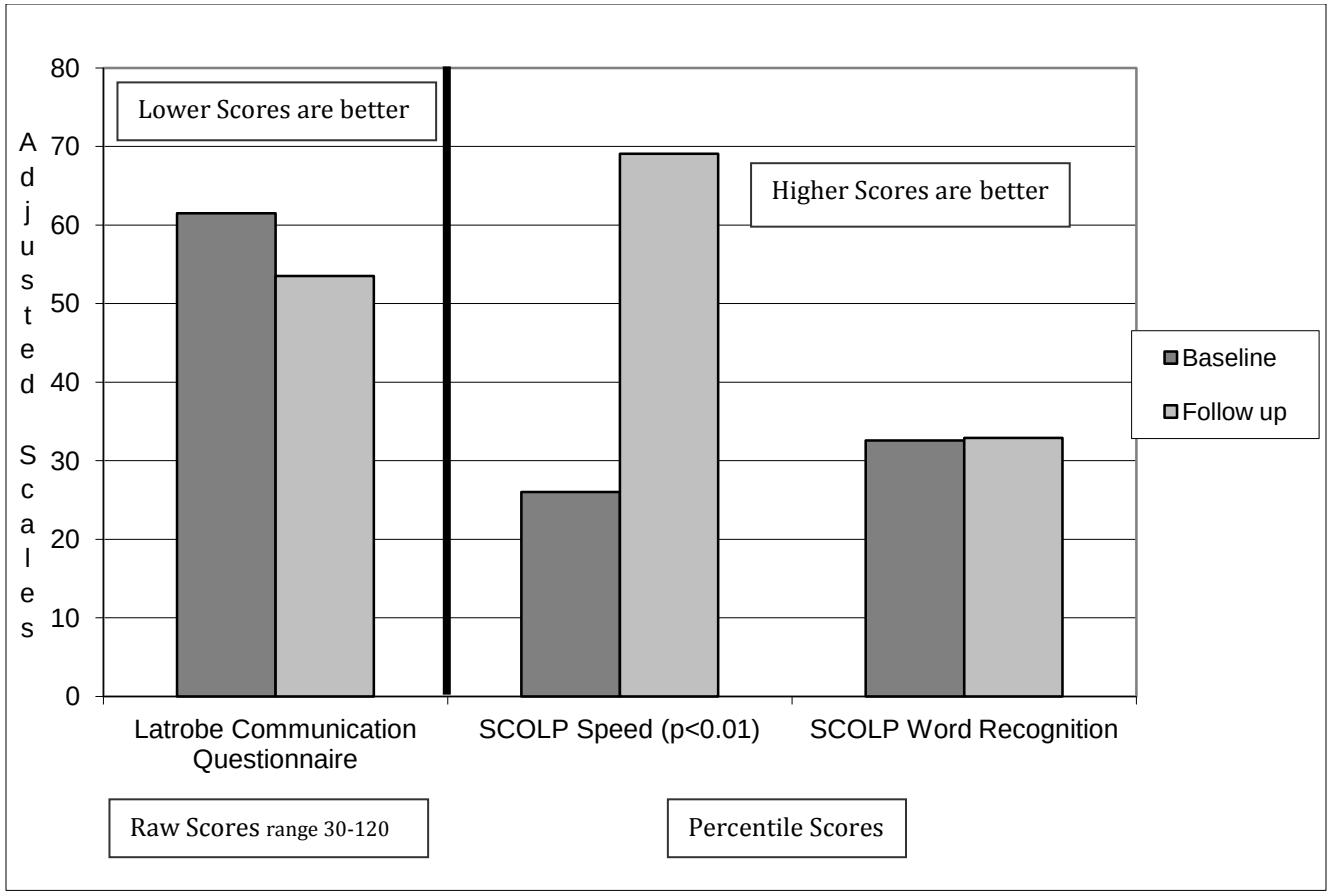


Figure 5. **Results for communication scales (N = 12).**

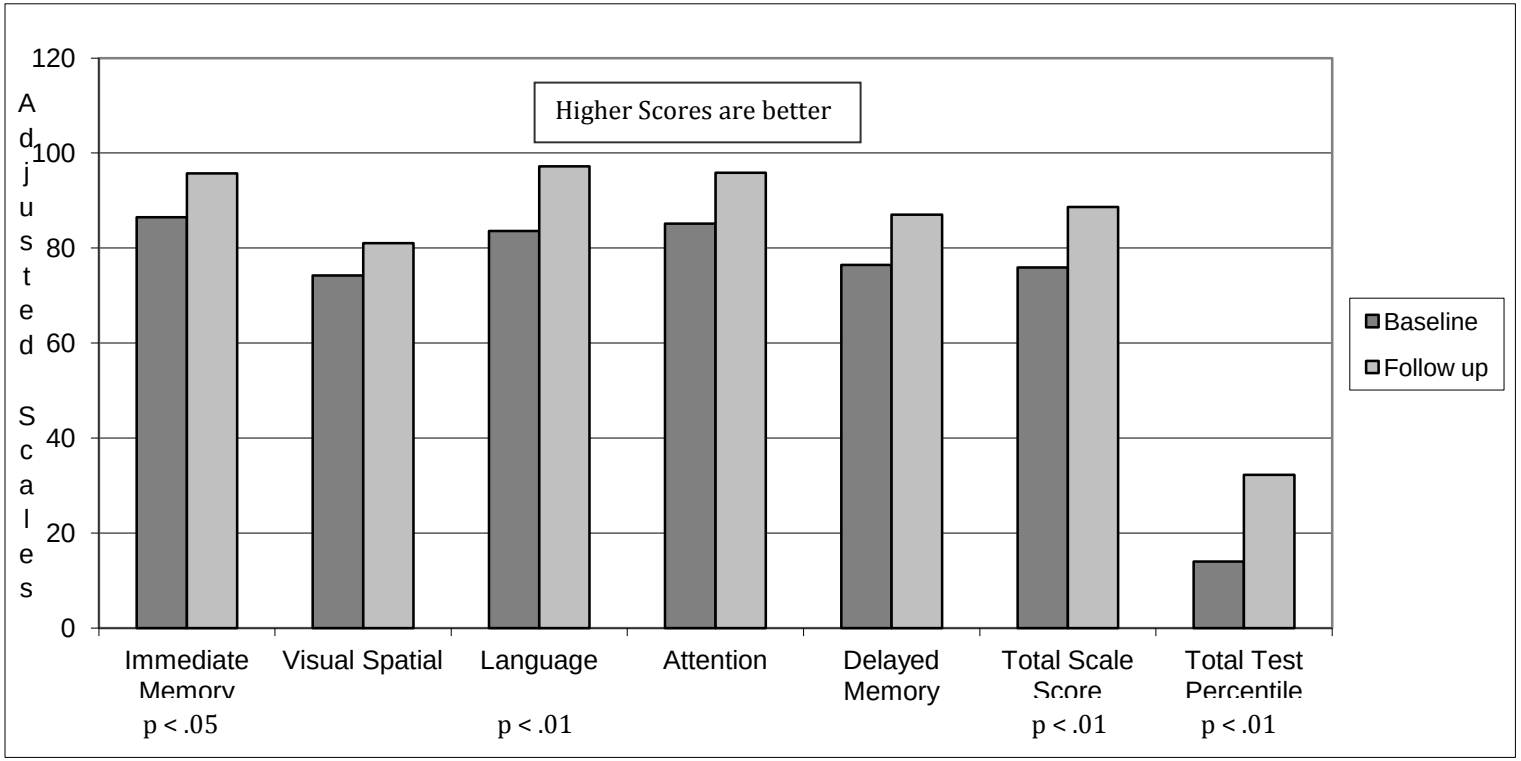


Figure 6. **Results for repeatable battery for the assessment of neuropsychological status (RBANS; N = 12).**

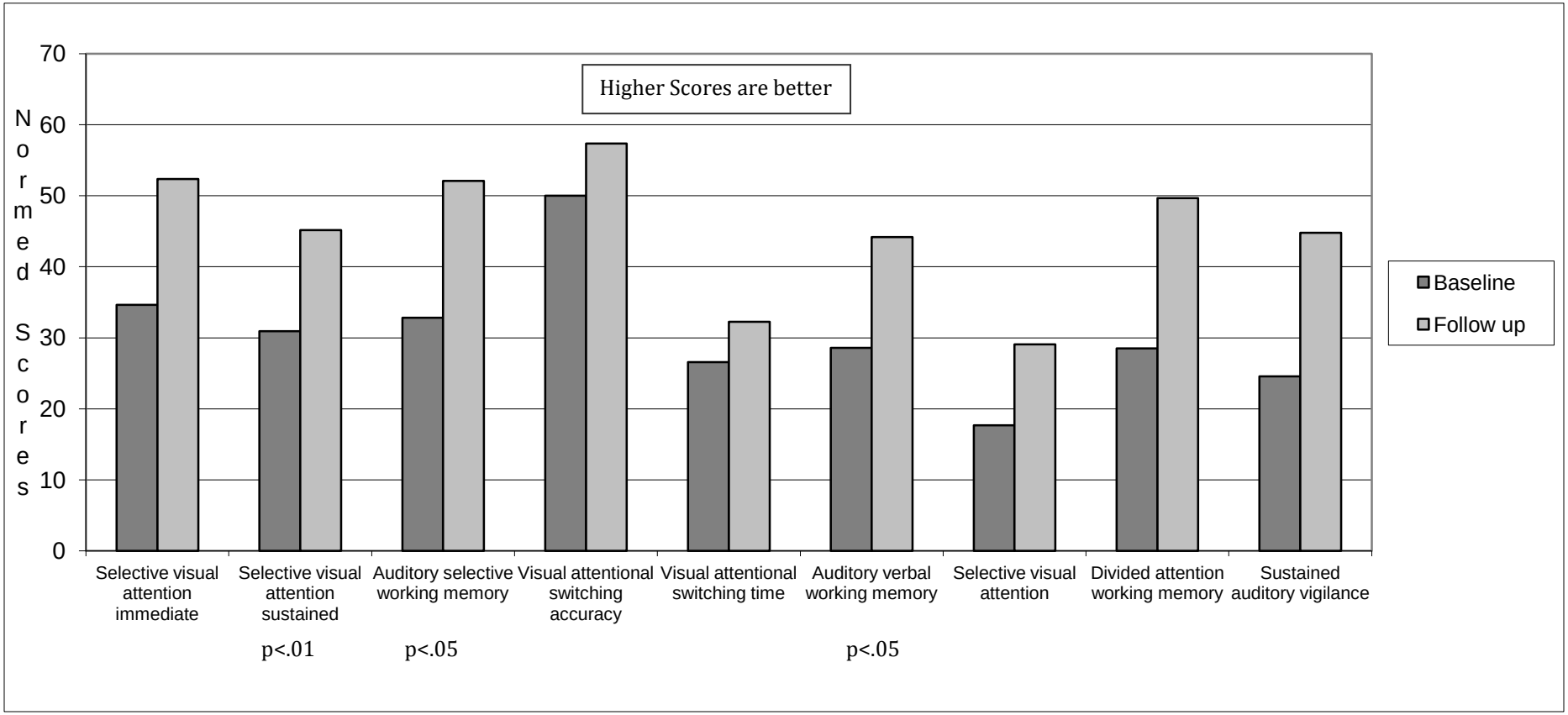
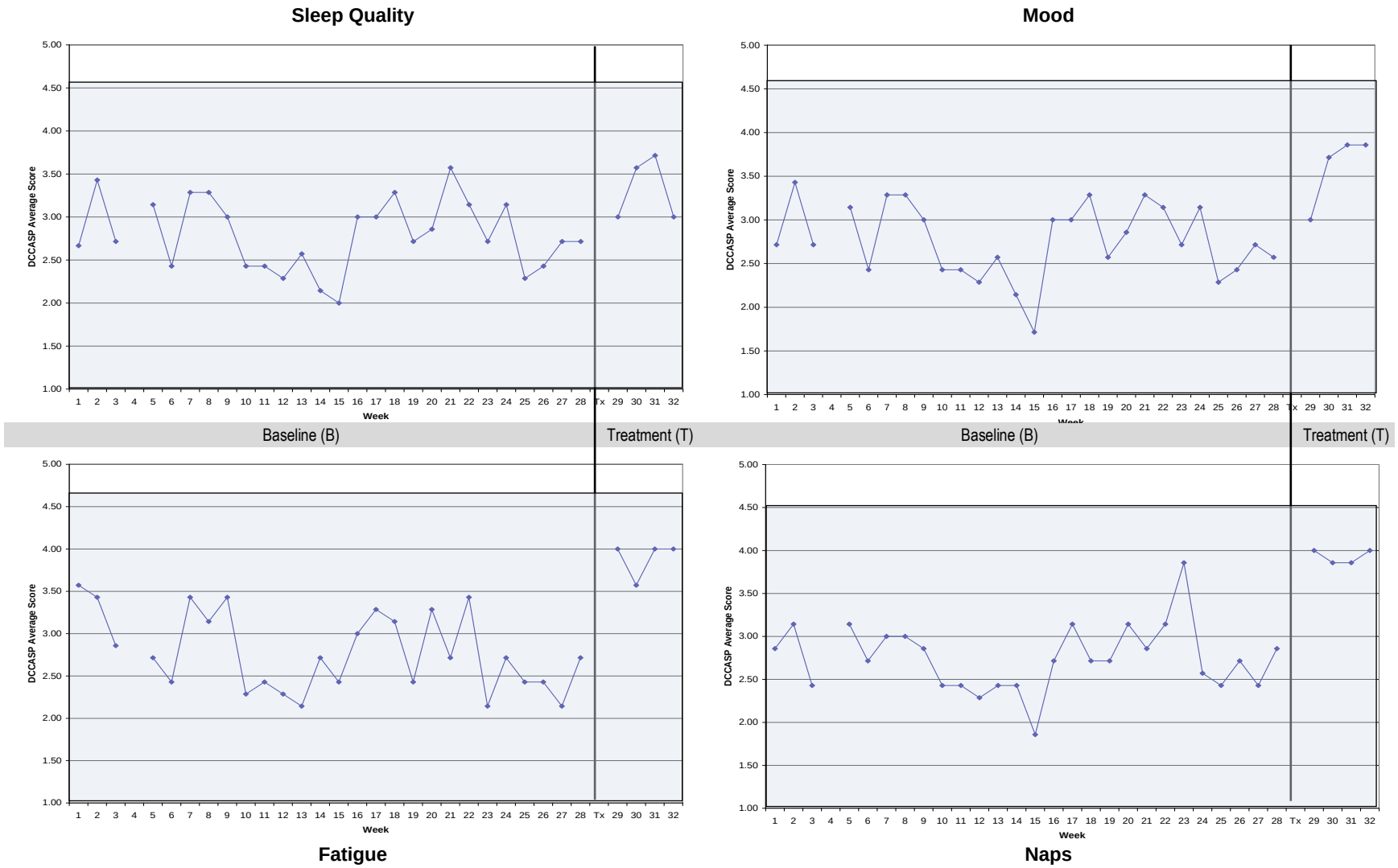


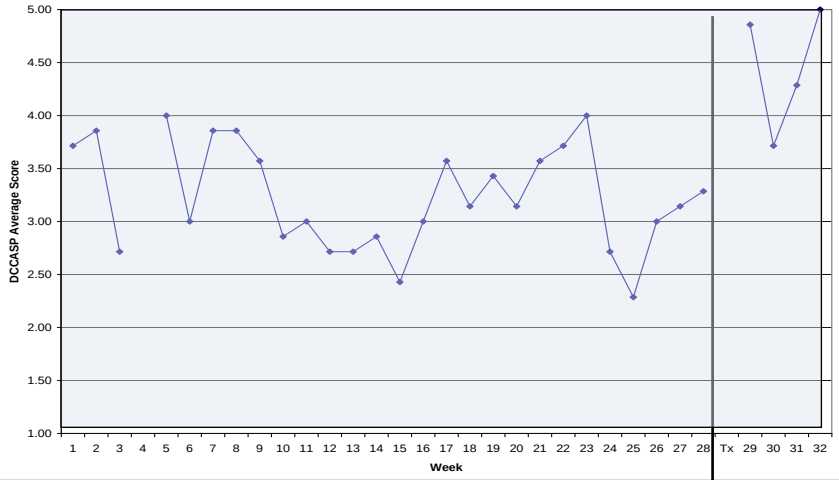
Figure 7. **Results for test of everyday attention (TEA; N = 12).**

Participant 1



Participant 1 cont'd

Attention



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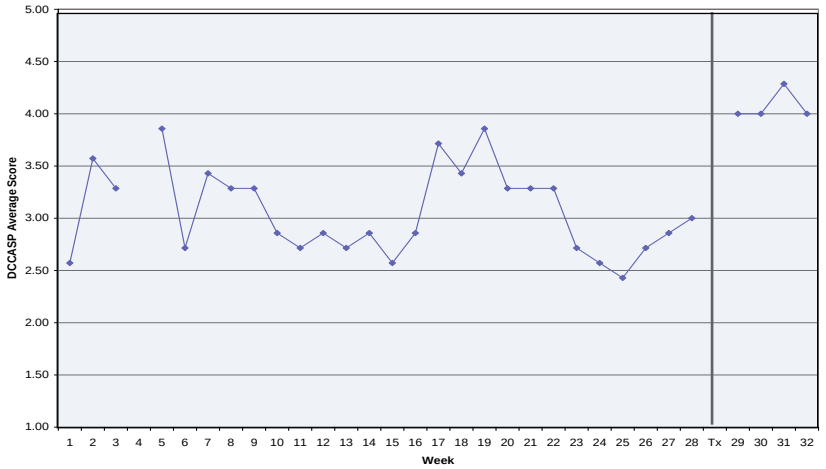
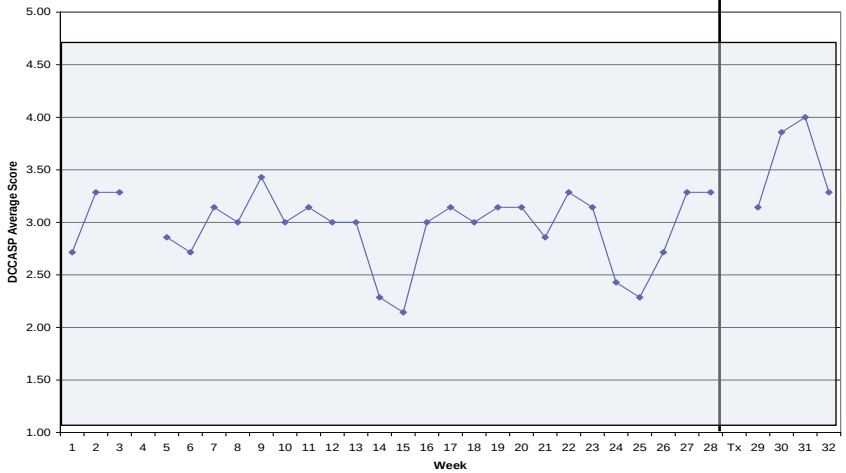
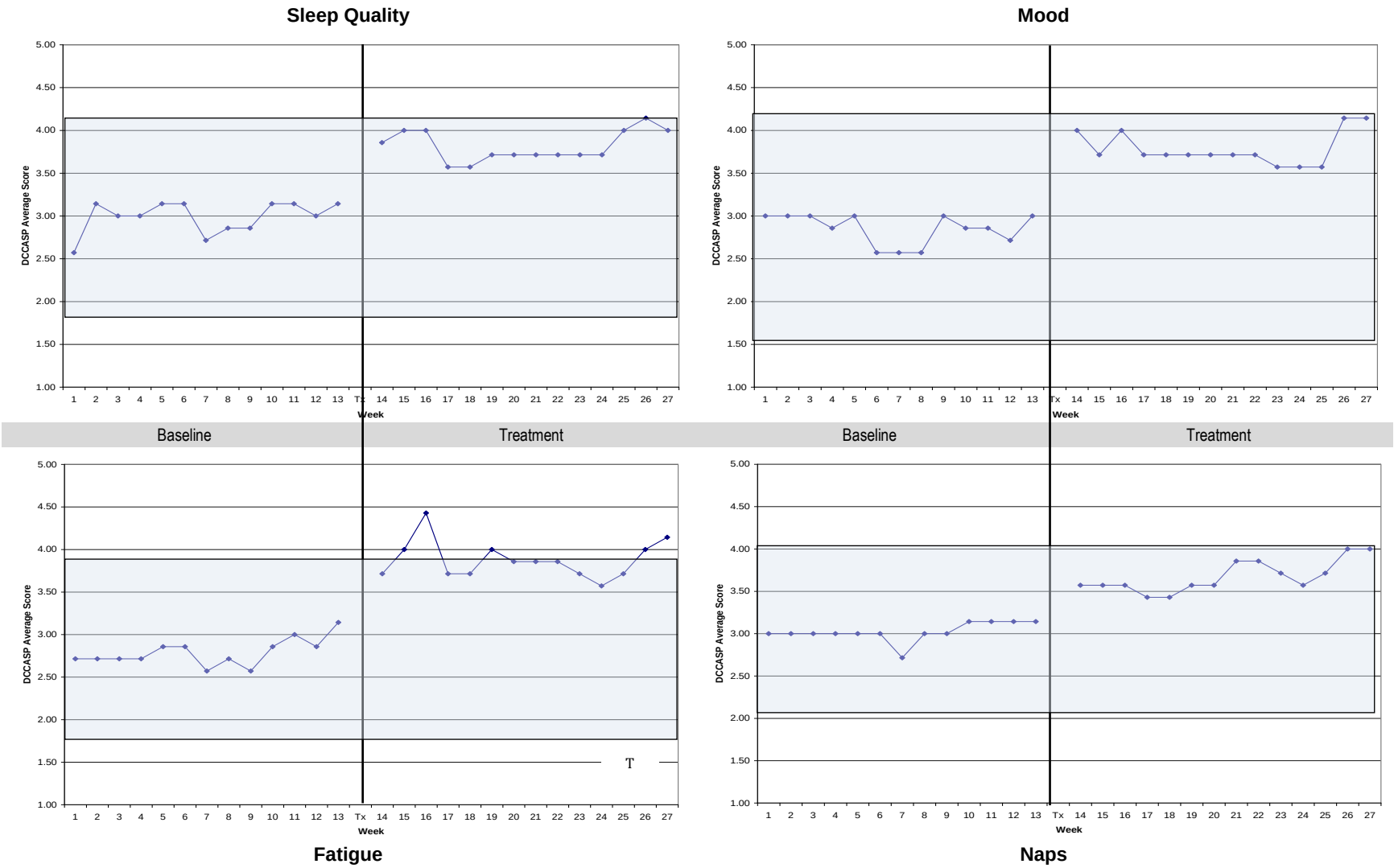


Baseline (B) Treatment (T) Baseline (B) Treatment (T)



Language Processing

Participant 2



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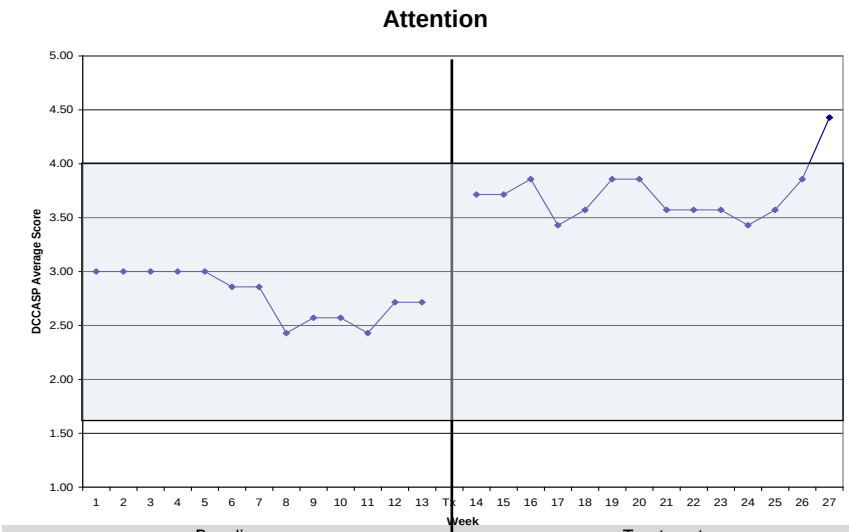
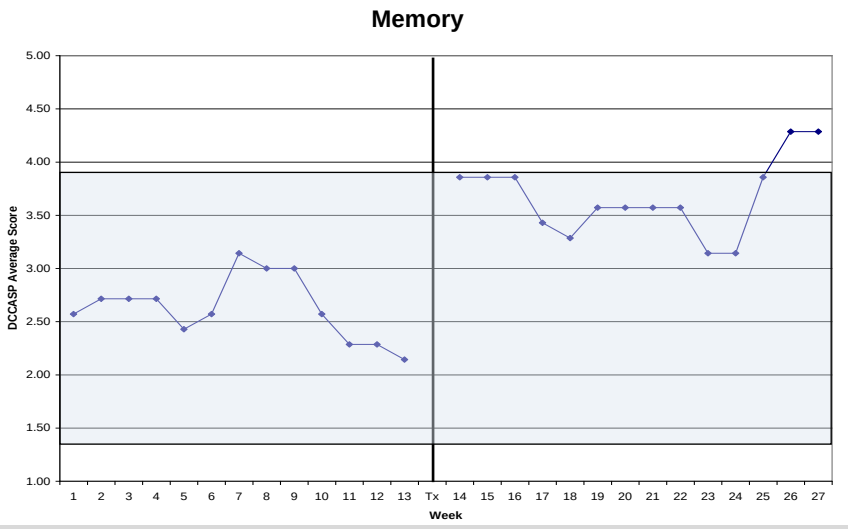
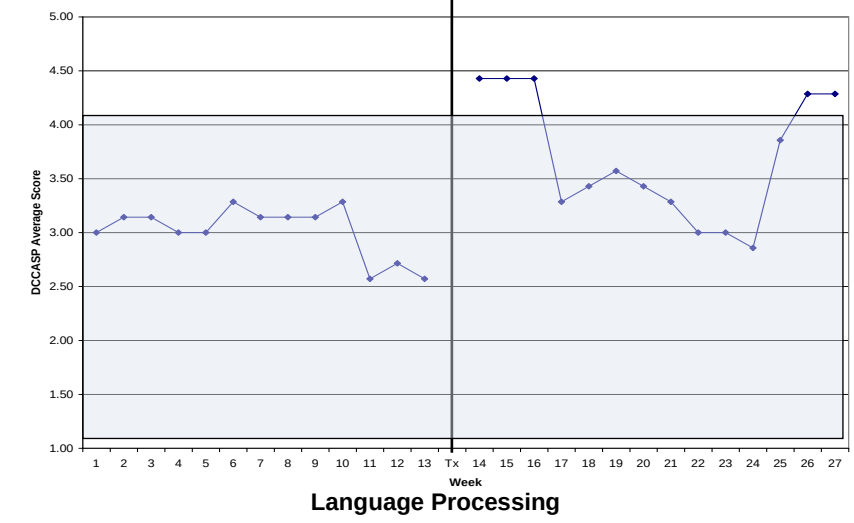
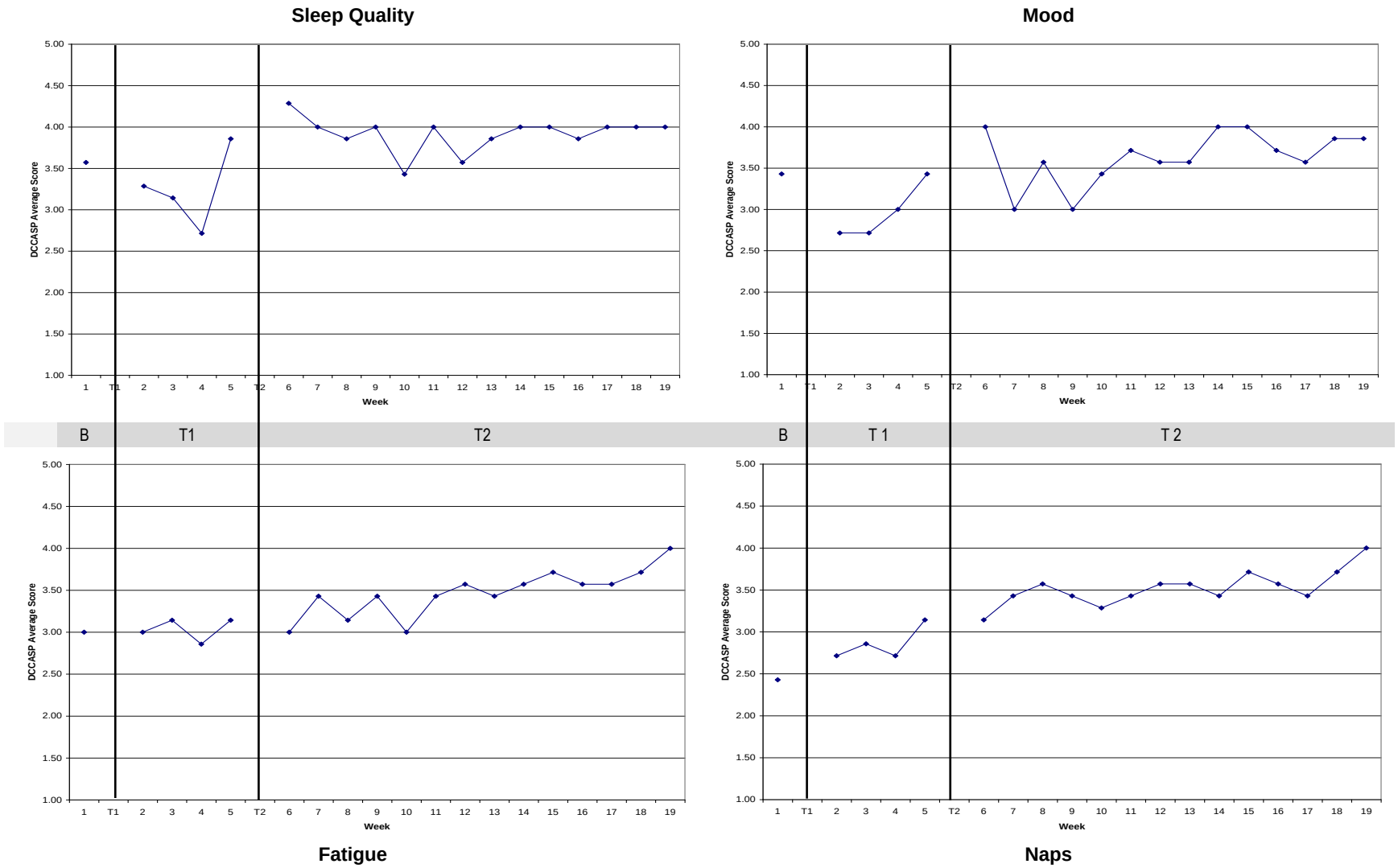






Participant 4



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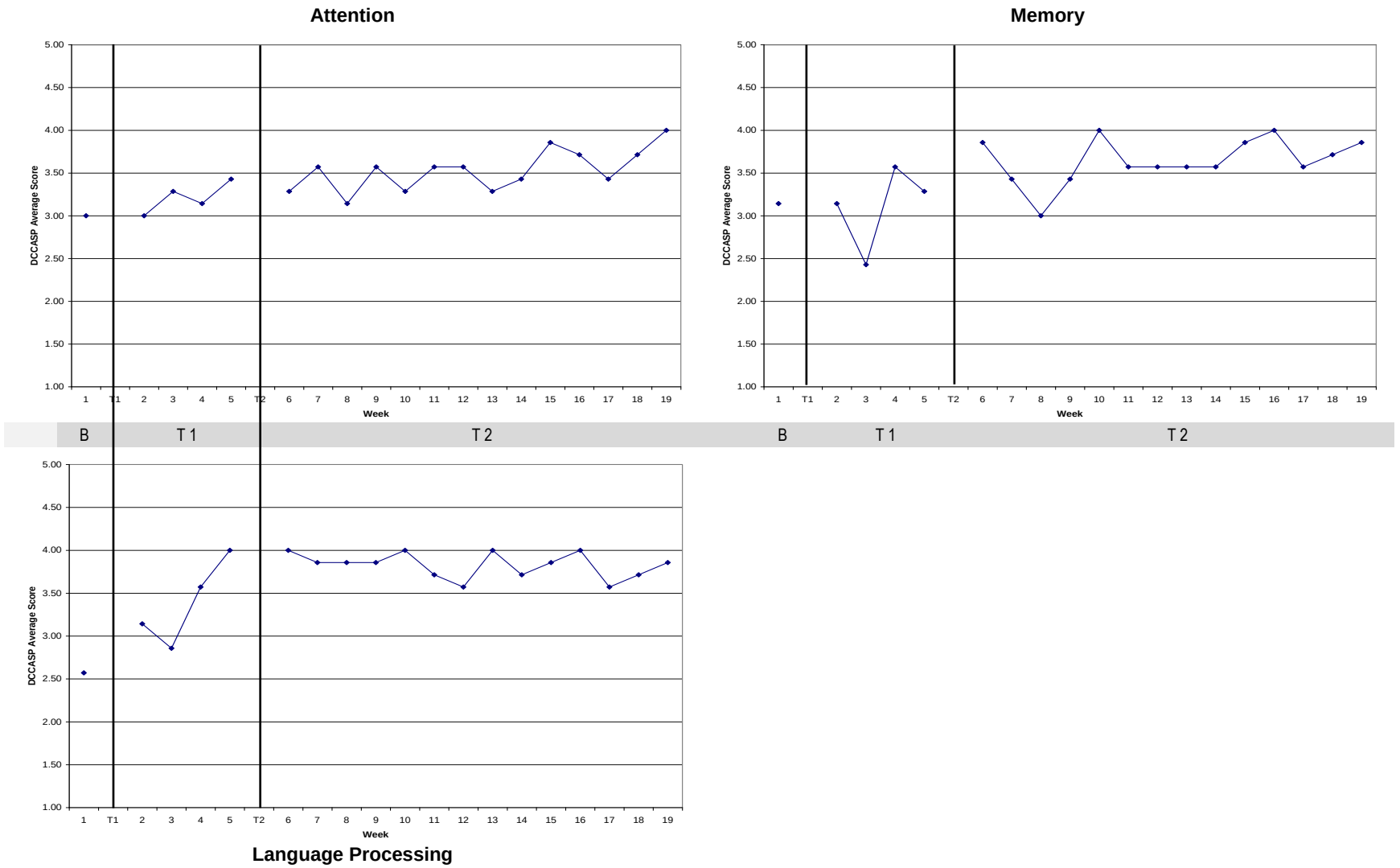
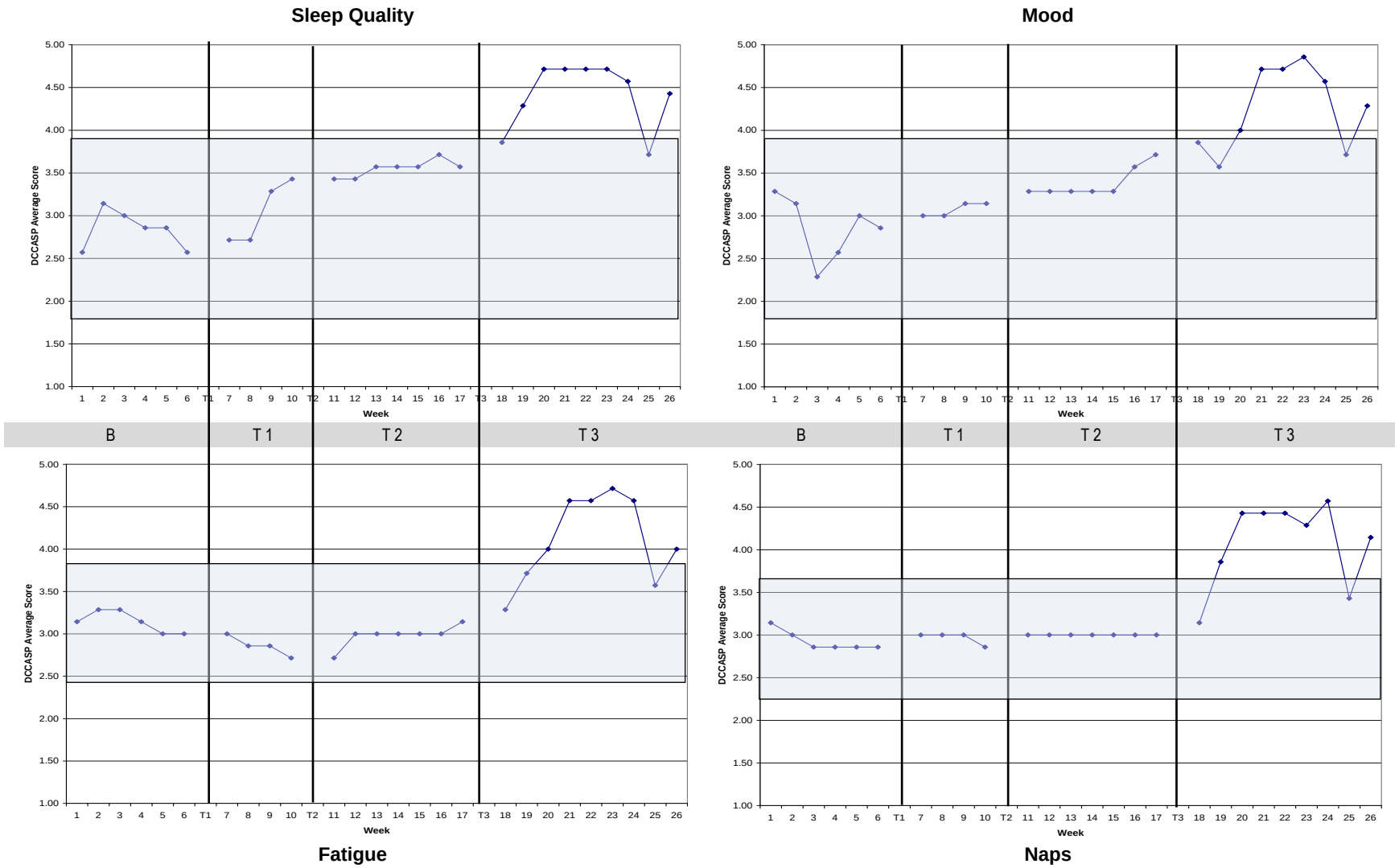


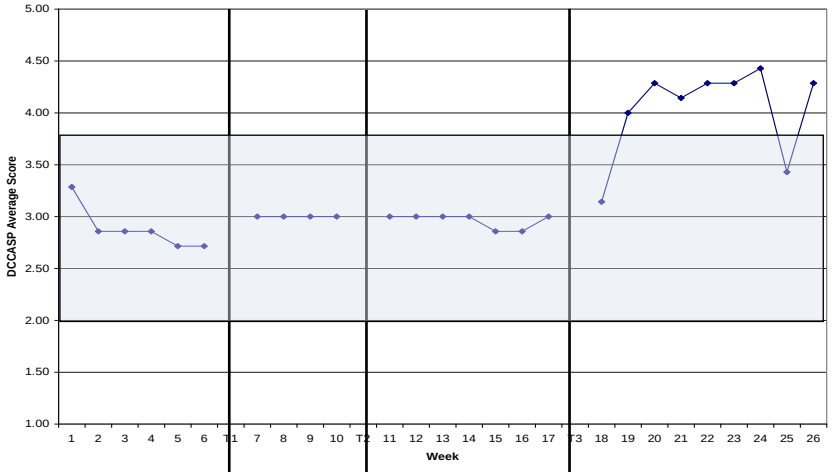
Note. No 2SD band analysis due to shortened baseline.

Participant 5



Participant 5 cont'd

Attention



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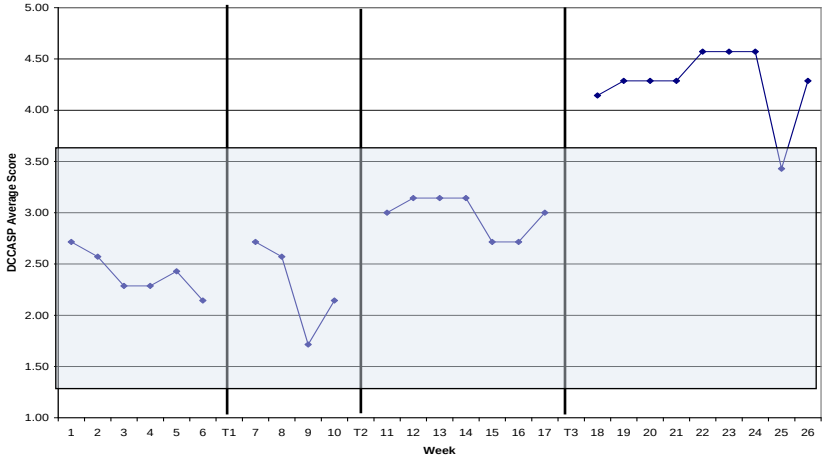
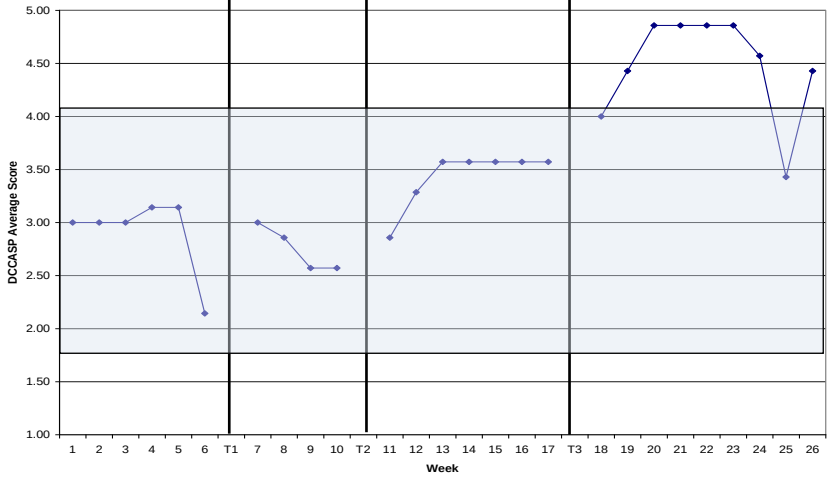
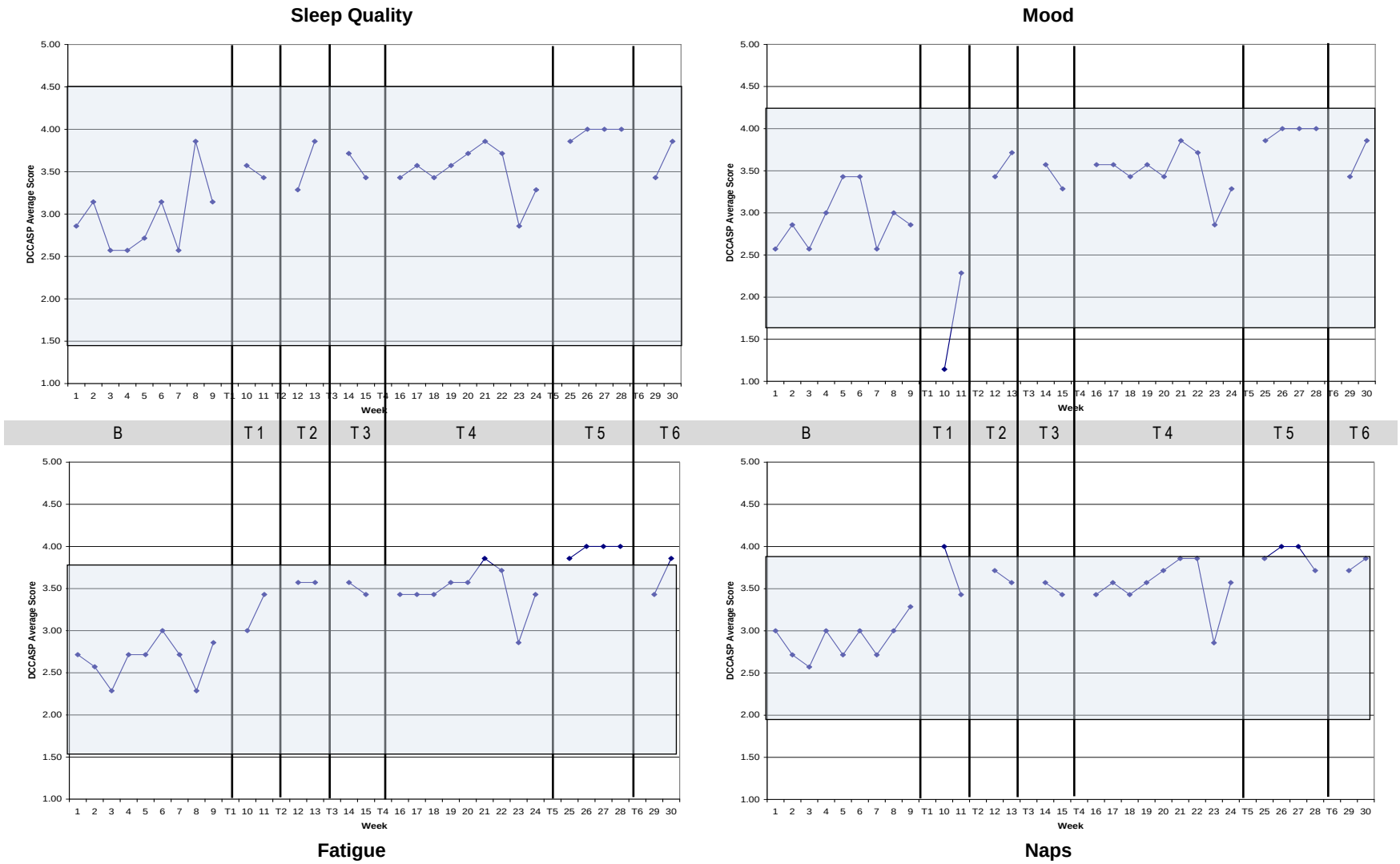




Language Processing

Participant 7



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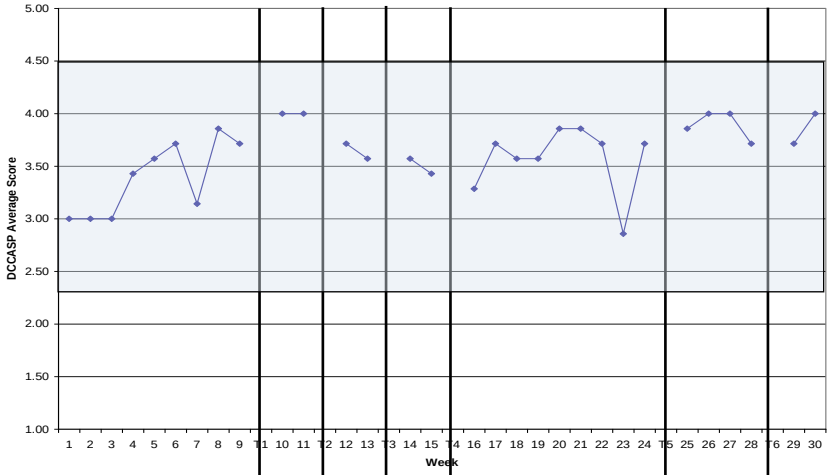

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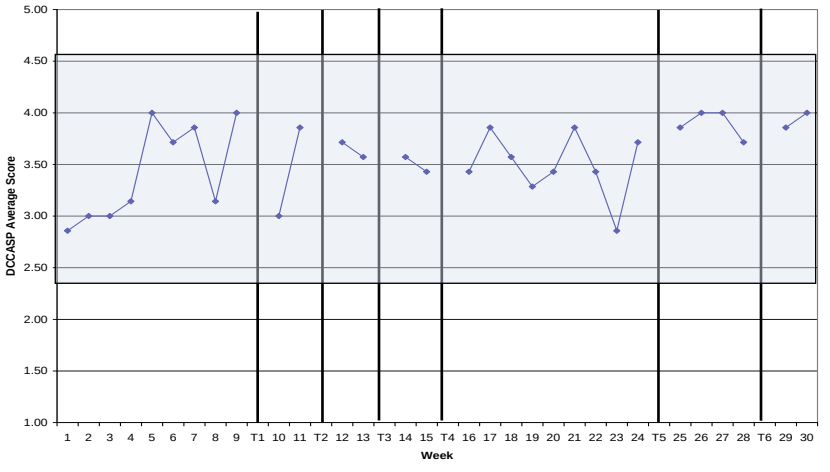
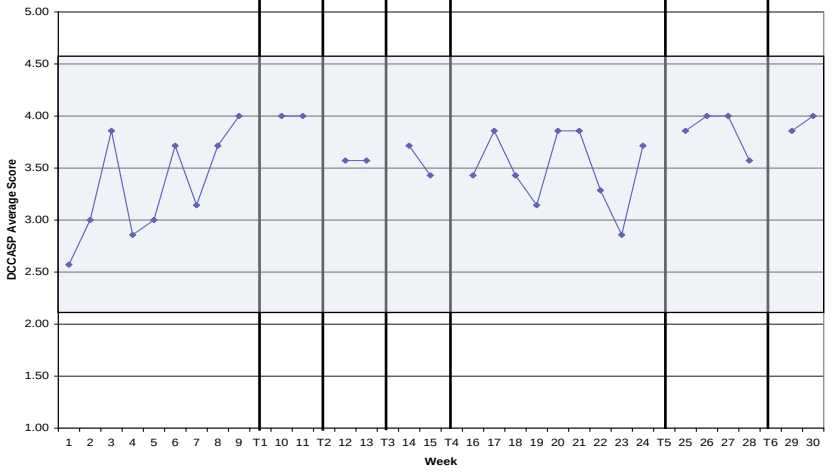
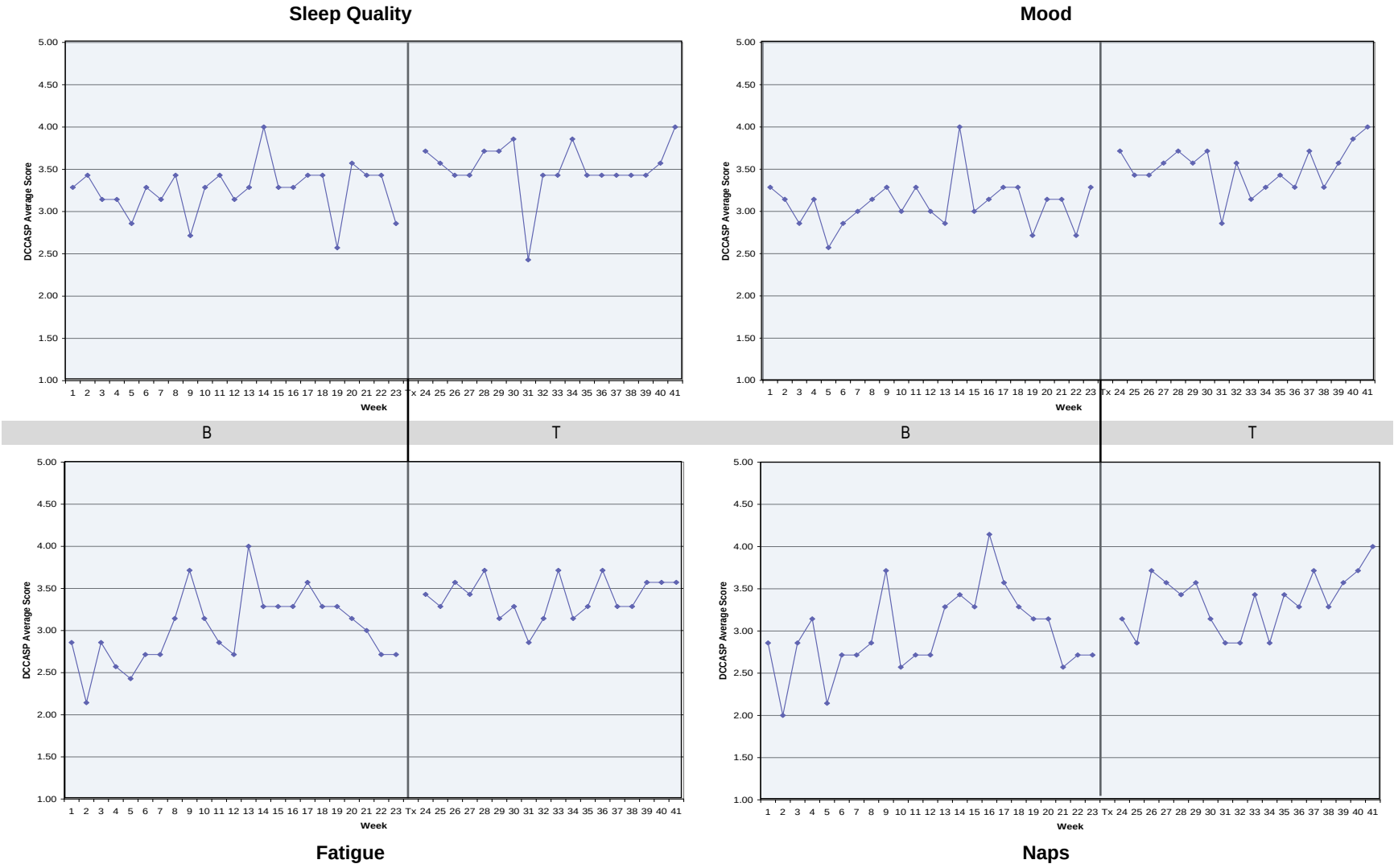




Language Processing

Participant 9



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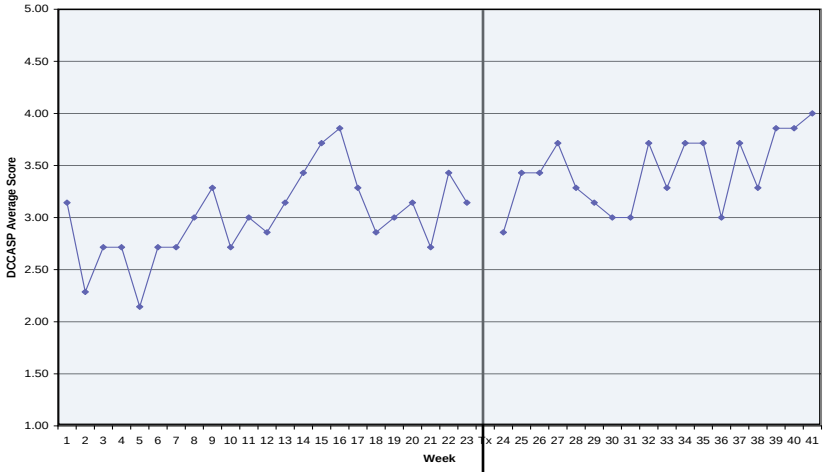

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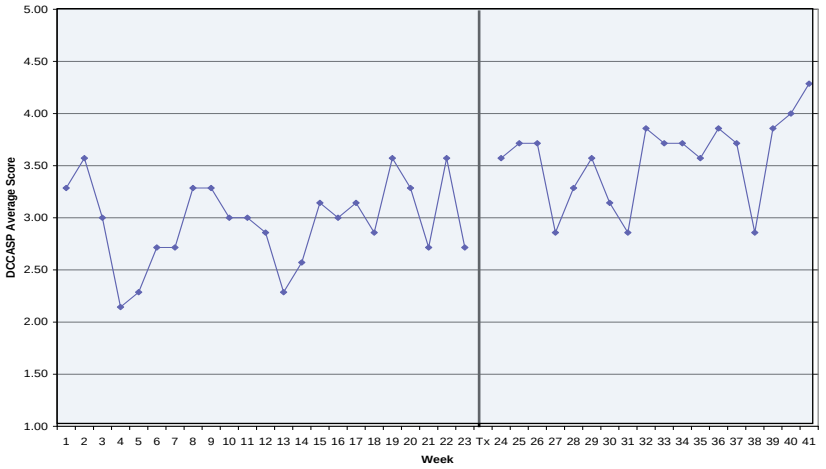

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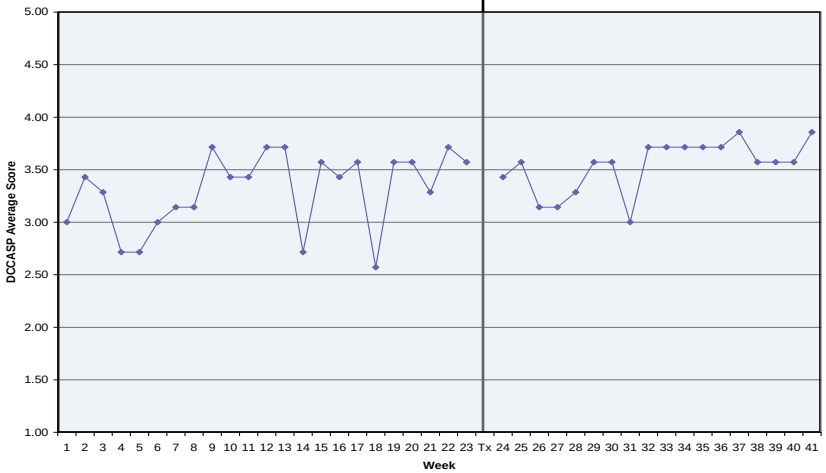
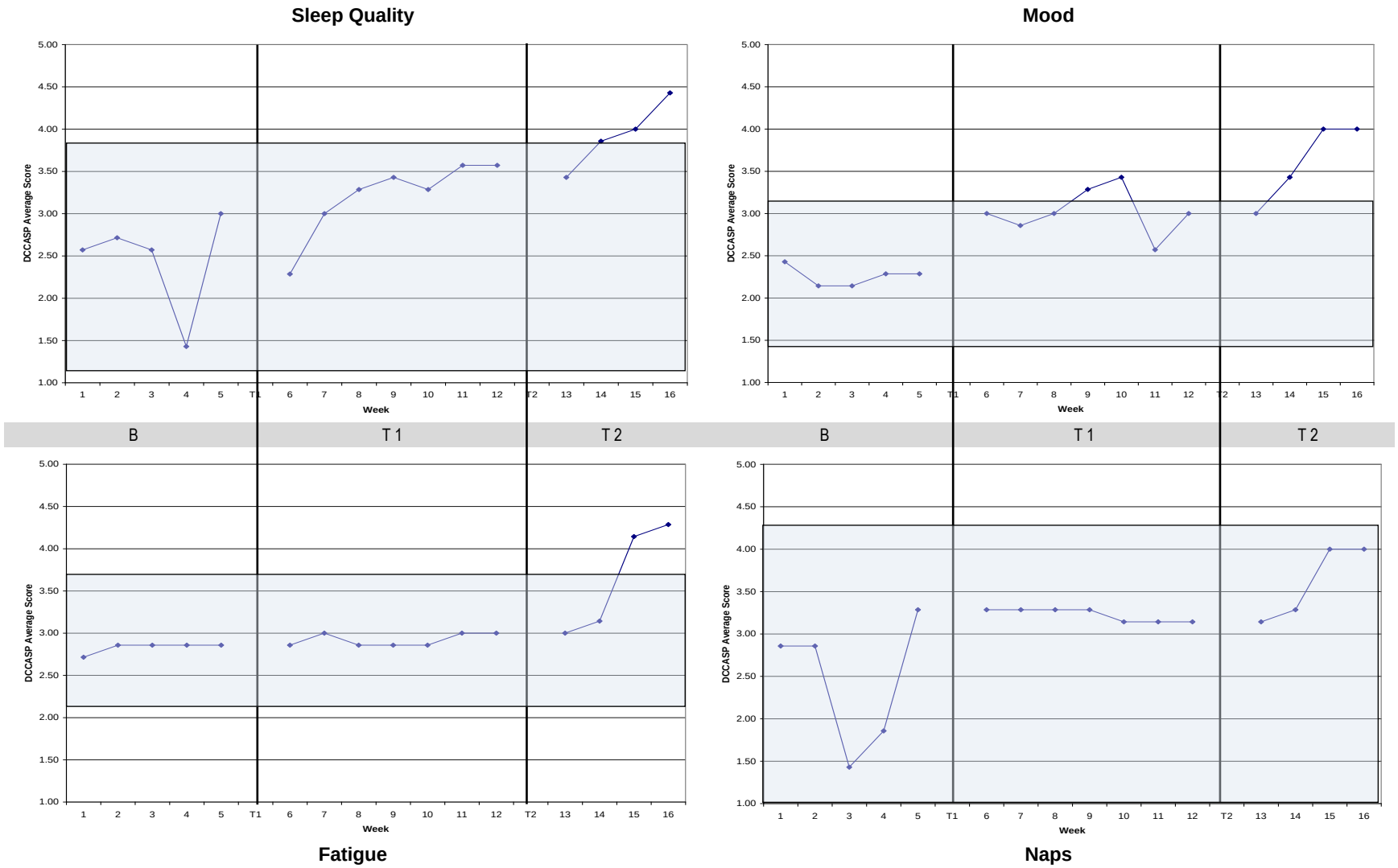


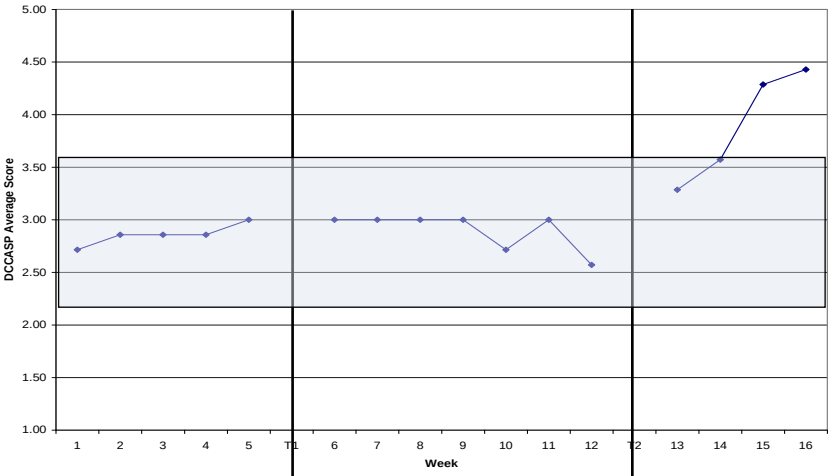
Language Processing

Participant 10

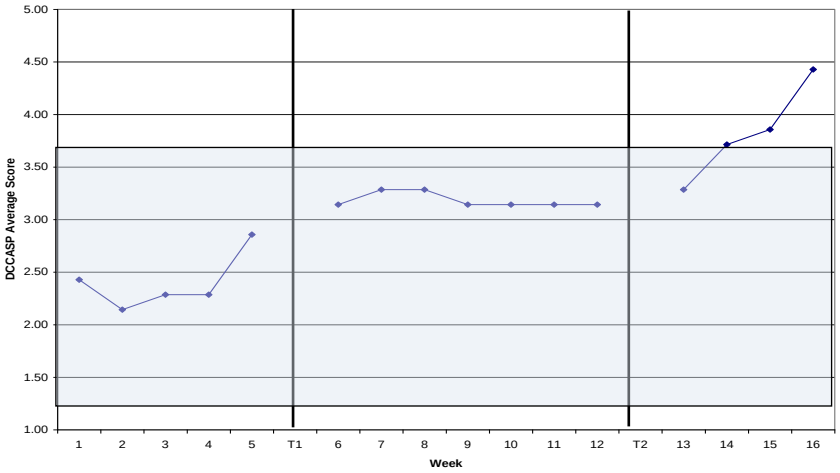


Participant 10 cont'd

Attention



Memory



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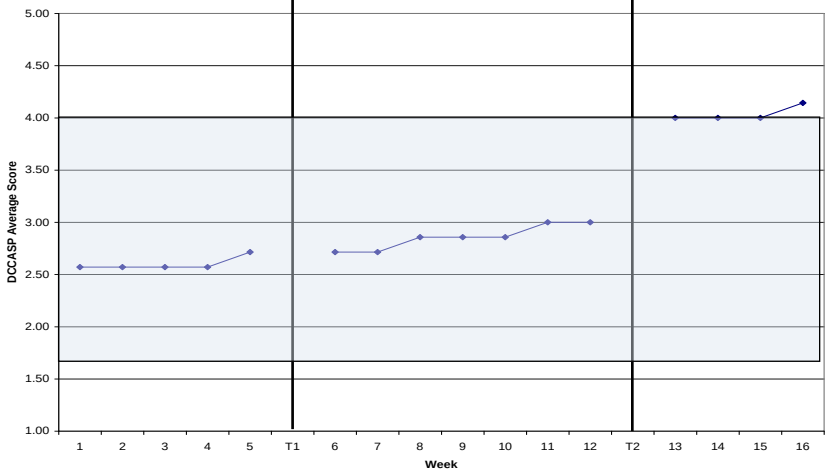
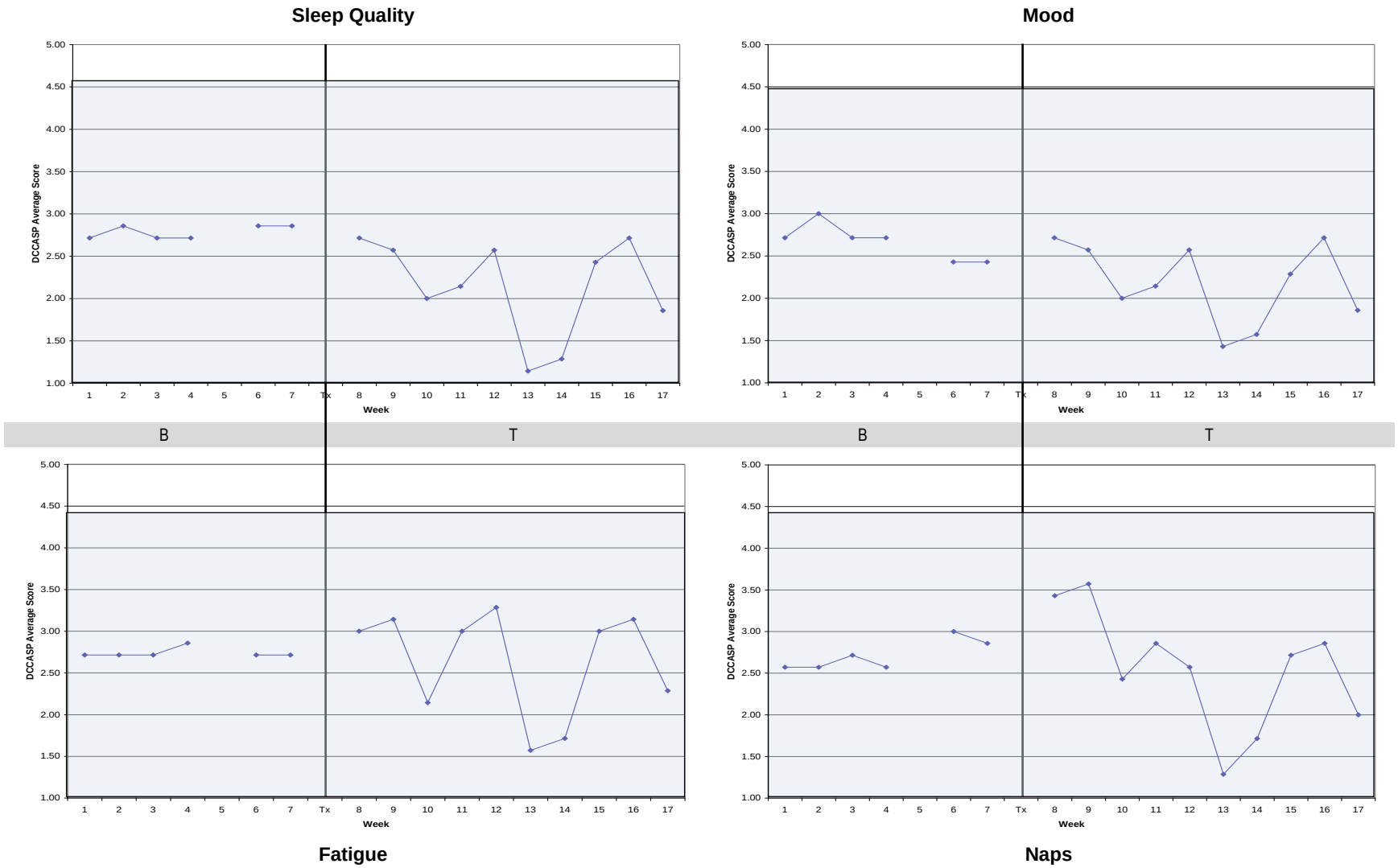


Language Processing

Participant 11



Participant 11 cont'd

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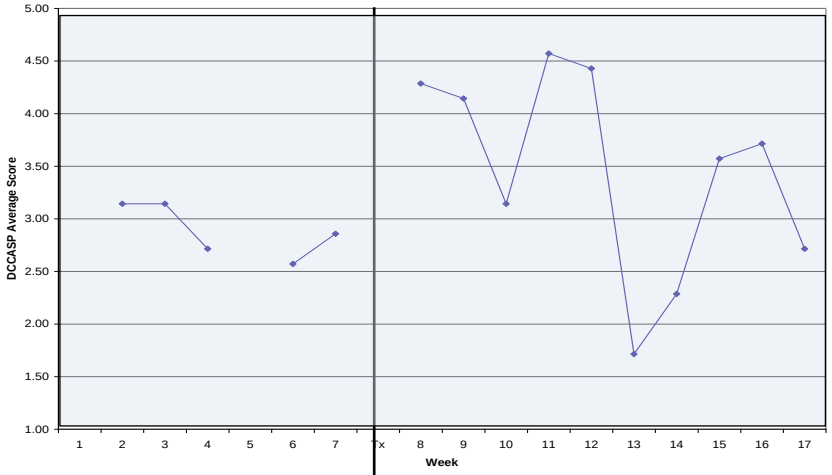

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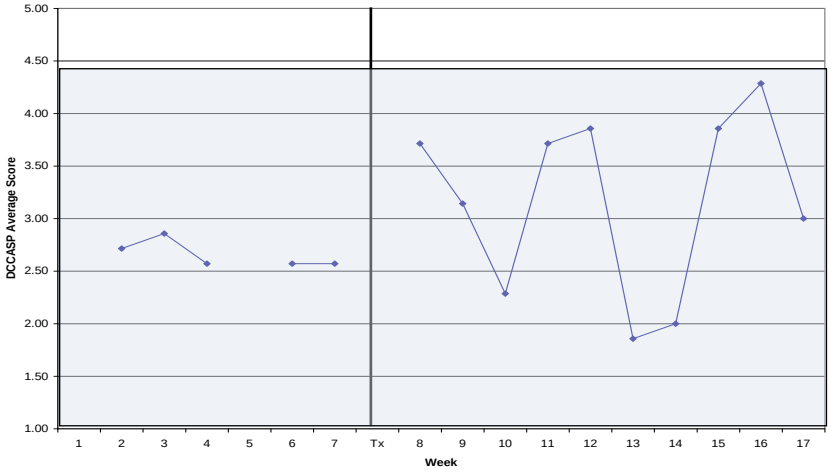

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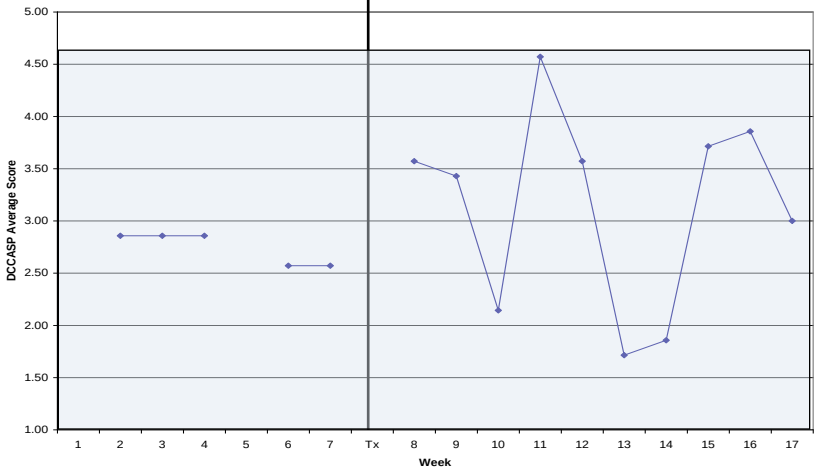
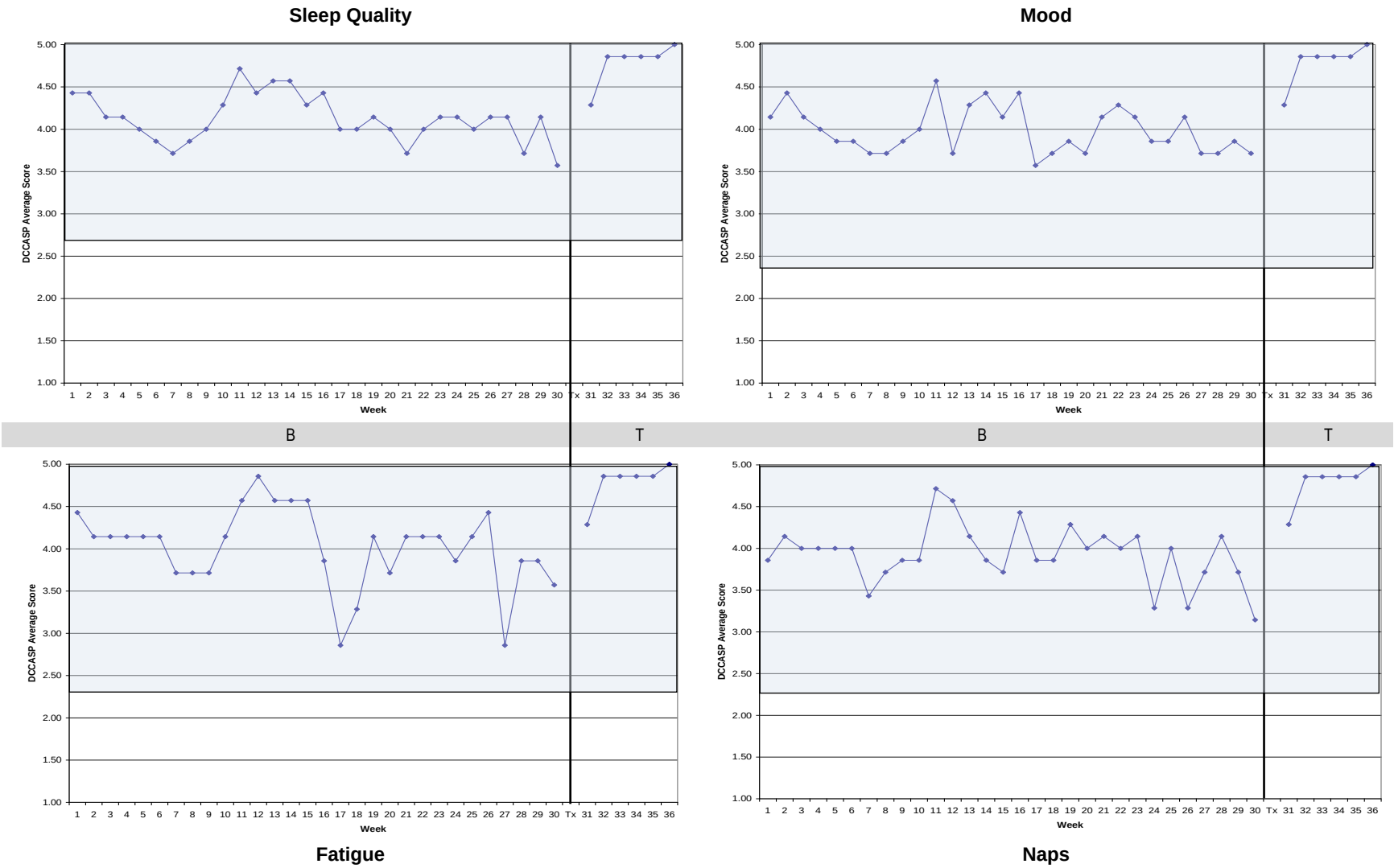


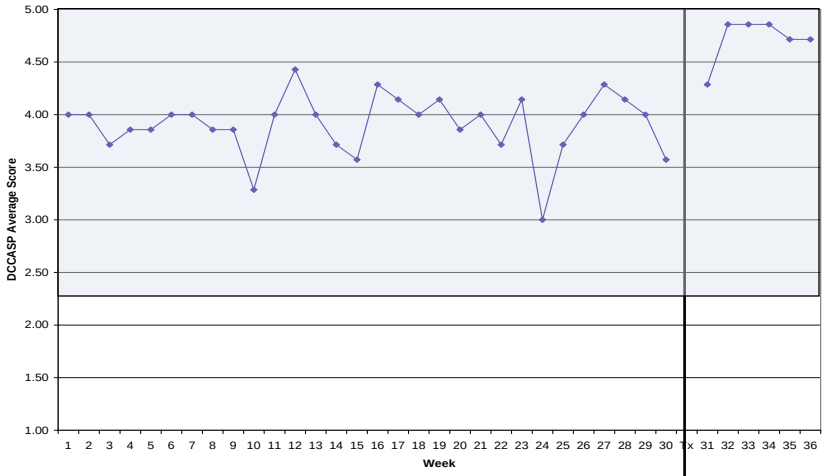
Language Processing

Participant 12

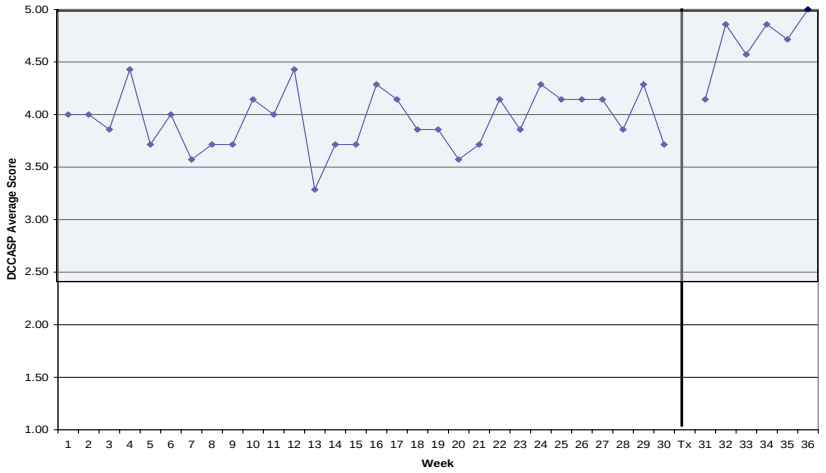


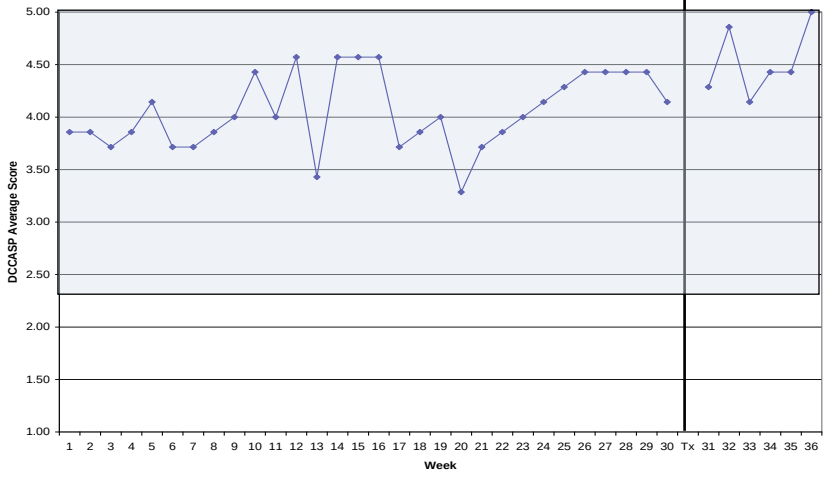
Participant 12 cont'd

Attention



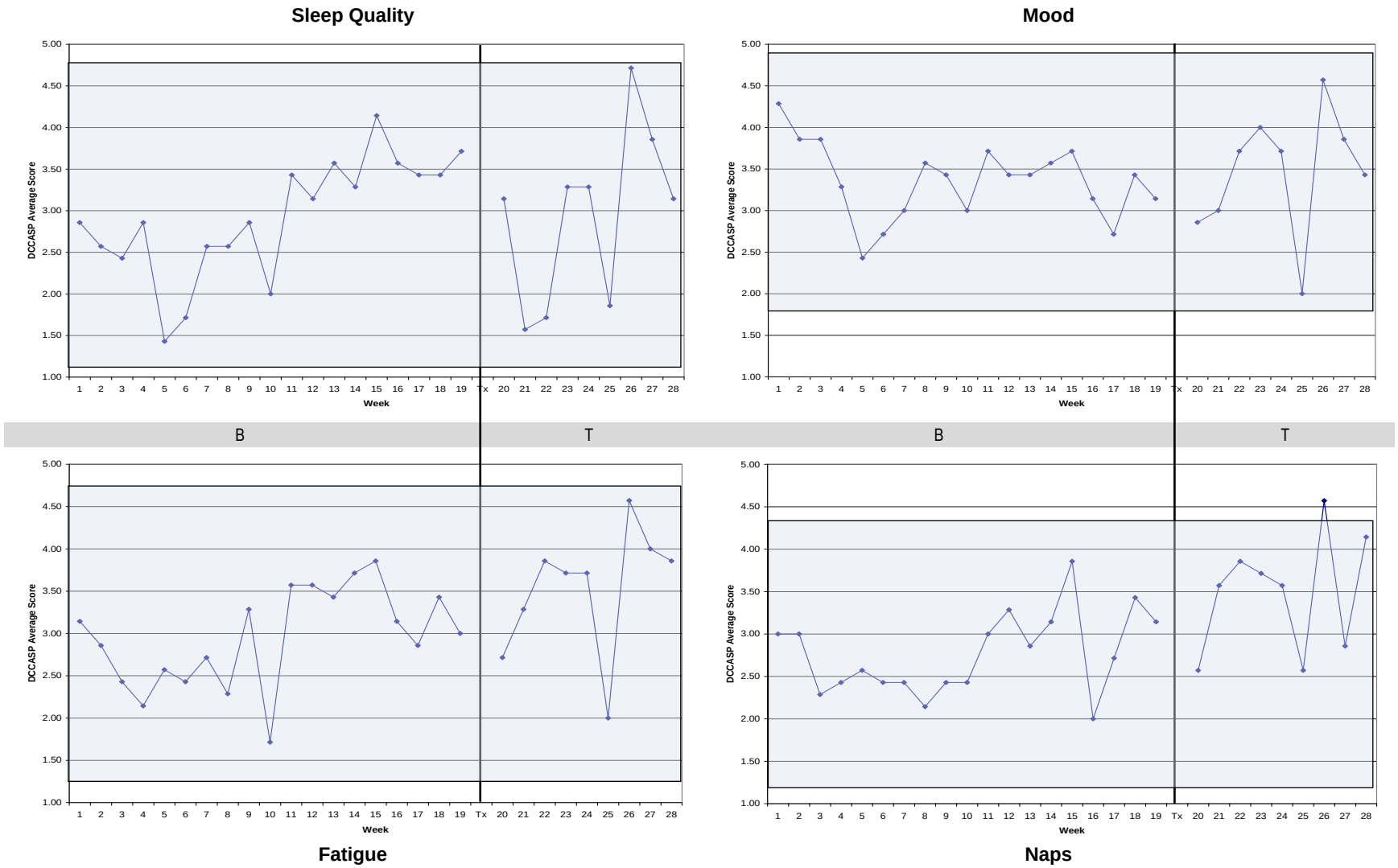
Memory





Language Processing

Participant 13



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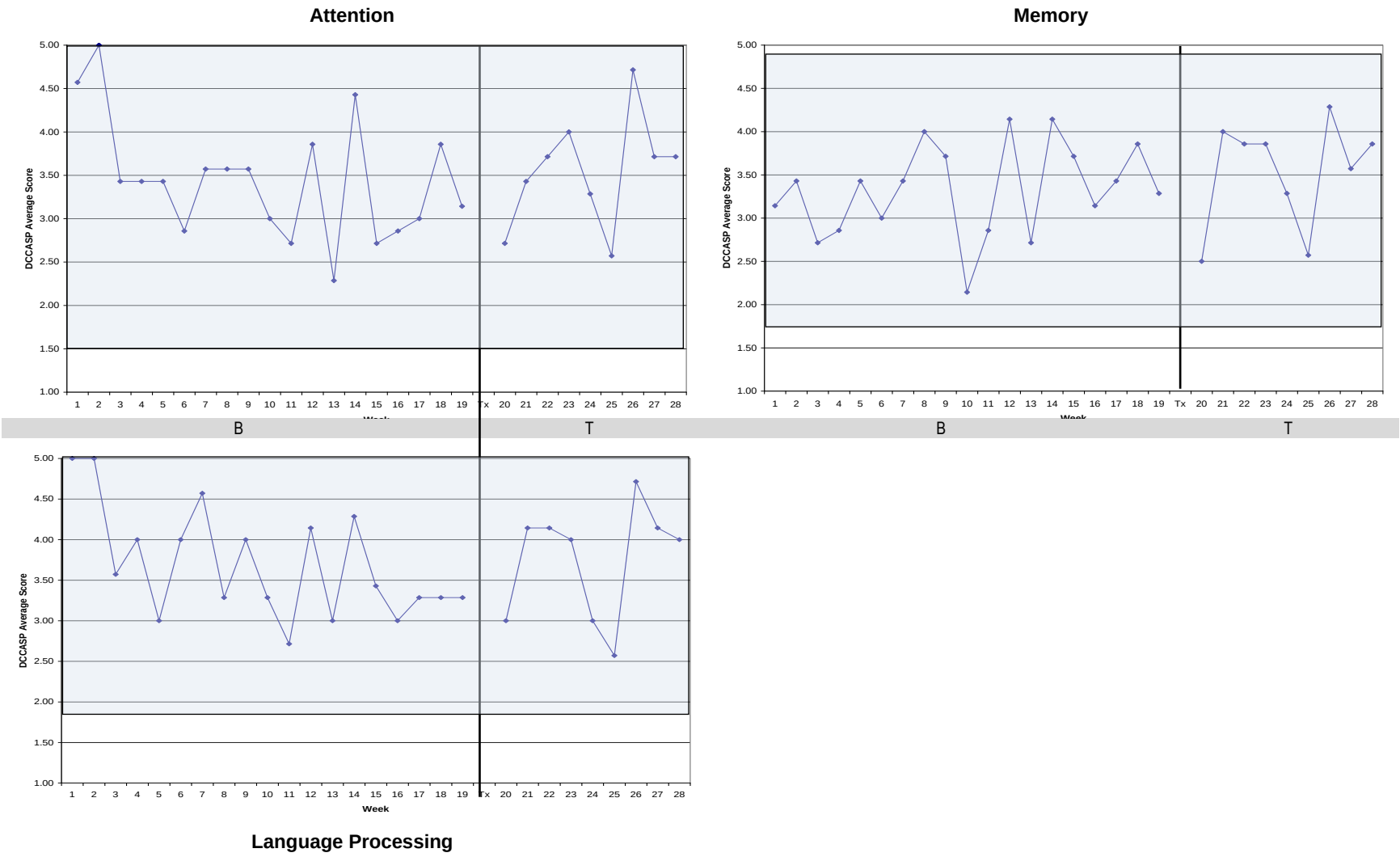

Figure 8. **Title DCCASP average score by week with 2 standard deviation bands for participants 1, 2, 4, 5, 7, 9-13.**

Note. Participant 3 was loss to follow up so baseline sleep data only, participants 6 & 8 were unable to complete the DCCASP due to response burden (even though support was provided).

4.4 Discussion

This study builds upon the previous case study results published by Wiseman–Hakes et al. (2011). To our knowledge, collectively these are the first studies to examine the impact of treatment of sleep and wake disorders associated with TBI, on recovery of cognition, communication and mood.

The findings of this study highlight the considerable heterogeneity and complexity of sleep and wake disorders among the TBI population. Our results suggest that the proper identification, diagnosis and treatment of sleep and wake disorders associated with TBI can facilitate, and in come cases, optimize outomes. Our findings suggest that proper treatment of sleep and wake disorders, may optimize recovery from cognitive and communication impairments in the areas of sustained attention (vigilance), divided attention, working memory, and speed and capacity of language (and information) processing, even for those individuals many years post-injury. All participants, regardless of their stage of recovery, showed clinically and functionally relevant improvements and in some cases statistically significant improvements across all measures in response to intervention. It is also important to note that the objective of this study was NOT to determine treatment efficacy or methods of treatment, but rather, to examine the impact of treatment on cognitive and communication outcomes. Thus, our results also suggest that communication competence and mood may be enhanced in response to optimization of sleep and wakefulness. This was emphasized by the results of 1 participant with both apnea and insomnia. As reported above, this individual was successfully treated for the apnea, however continued to present with severe sleep maintenance insomnia. Subsequently this individuals' depression score worsened from moderate to severe by the end of the study. Further, this individual reported that in the workplace, they felt as if they were functioning like someone '10 years their junior in regards to experience'; that information they would previously have processed quickly with limited time and effort (prior to the TBI and onset of the sleep disorder), was now slow and effortful, requiring intense concentration. This individual reported that they were unable to multi-task (a requirement of this individuals' work position), and professional communication interactions, particularly phone calls, could no longer be spontaneous, but required advanced preparation.

In contrast, another individual who was successfully treated for obstructive apnea, reported that they now slept for the first time in 18 years (since the injury). This participant reported that their "overall awareness was heightened (in a positive way)", whereas previously they "had been irritable and overly sensitive to stimuli", they now felt "calm and energized". This participant further commented with humour, that they were no longer as easily annoyed by people, stating that "I had decided years ago I really didn't like most people because they were quite frankly, annoying, but now that I am sleeping, I have mellowed quite a bit and am less easily irritated. The downside of sleeping however is that now I have to have a 'waking-up process' instead of simply hitting the ground running! You have to realize that sleeping is new to me. I literally did not sleep much for 18 years so sleep is new to me. Sleep and I are still in the honeymoon stage. I was not sure at first that I even liked sleeping but I think it is growing on me"! Further, through completing the DCCASP, this individual recognized how they had over-estimated their functioning prior to successful management of their sleep disorder. They reported that once they began to sleep, they realized that they had in fact, not been functioning well for 18 years, but rather that they had become extremely adept at compensating.

These findings are particularly important, in part because there is a misconception among many practitioners that insomnia following TBI is directly related to brain damage, and thus cannot be treated (unlike other sleep disorders) or, that it will improve with time. Furthermore, the awareness of the prevalence of sleep and wake disturbance associated with TBI has been heightened recently, however the majority of individuals with these disturbances are suffering in silence, and these problems are not being addressed. It was telling that although this study was conducted in Ontario, Canada, we had requests to participate from as far away as British Columbia and Saskatchewan. This may be an indication of lack of or, limited accessibility to comprehensive evaluation and treatment of sleep wake disturbances for individuals with TBI.

Although our study design did not allow us to establish clear, causal relationships, our findings do highlight the critical relationship between sleep, mood, cognitive function, and communication competence. All of these areas are often compromised following TBI, and

so by failing to screen for and treat sleep and wake disturbances, patients may not be able to reach their full potential for recovery.

4.4.1 Study Limitations

Given our small sample size and lack of control group, our findings may not be generalizable to a larger population of individuals with TBI. Further, we were not able to conduct follow-up polysomnograms on our participants, which would have been helpful to look at any objective changes in sleep in response to intervention. As well, we did not have access to cognitive behavioural therapies for insomnia, which may have heightened the success of some of the interventions. Non-specific factors unrelated to the intervention such as changes in employment status, levels of stress, illness, were not formally accounted for in the results, however this information was collected daily via the DCCASP, and associated with short-term variations in perceived function in response to these factors. We recognize that our study design did not allow us to formally control for a possible placebo effect however we did a significant stable baseline period of at least 1 month for virtually all participants.

The study measures were carefully chosen from the existing battery to evaluate aspects of cognition, communication and mood that are sensitive to restrictions in and changes in sleep. As with any assessment there is no 'ideal battery', and each measure had its strengths and weaknesses. In retrospect, the measures used are still deemed to be the best possible assessment battery and captured both objective processes and self-report, and were ecologically valid. Like any battery, the objective measures may not have been sensitive enough to pick up subtle cognitive deficits in those very high functioning participants and so a ceiling effect was noted for some measures at the baseline administration. The Daily Cognitive-communication and Sleep Profile (DCCASP) also has a heavy response burden as it should be completed daily (although it only takes 5 minutes) and, some participants required regular support to complete it. Two participants were unable to complete the DCCASP, one due to significant memory impairments, and the amount of support required, and another due to fatigue and the response burden. However all those who did complete the DCCASP found it educational and informative. This does

however, add another potential confound to our results in that this heightened awareness may have added a response bias to particiants' perception of the relationship between their sleep and function, and this could possibly be interpreted as a placebo effect. The study was quite 'measure intensive' although the addition of a sensitive quality of life measure and a measure of occupation may have been helpful as we observed positive changes in these areas. Further addition of formal participation measures would also have been of benefit as we saw changes in participation. We also did not have information regarding site of injury for many participants; this information would have been helpful in providing some possible explanations of impact on cognitive-communication skills such as auditory processing and language.

The range of time that participants were involved in the study also varied greatly. Participants were actively followed for about 1 month after their sleep and daytime wakefulness was optimized, and were then seen for the follow-up neuropsychological and cognitive-communication evaluation. However all participants were seen again at 6-month follow-up or earlier if problems arose. Formal documentation for purposes of the study ended after the follow-up assessment. Participants were in the study an average of 8 months, and the range was from 4 months to 13 months.

Although our study was longitudinal, we assessed only relatively short-term impact. Participants were followed on average throughout the study for 8 months; however, they continued to be followed at regular intervals in the sleep clinic. Furthermore, the characteristics of our participants in this study are comparable to other studies of individuals with TBI. Males and females were equally represented across all age groups and different times post-injury. Future studies should include a larger sample size with age and sex matched controls, a follow-up polysomnogram, and longer term follow-up. In this study, the treatments were not experimental, but rather part of routine clinical care. An evaluation of the efficacy of various treatment approaches would also be of benefit.

We recognize that the design of this study with our heterogenous group of sleep disorders and cognitive profiles is such that we cannot determine causality through this investigation. However, determining causality is an important question for future research.

4.5 Conclusions

The polysomnographic and MWT results of this study showed sleep disorders to be highly prevalent in our sample at baseline. Although we recruited on the basis of self-report of sleep or wake problems, it was telling that our participants ranged from 1-22 years post-injury, and only one had had an assessment of sleep prior to participating in this study. Every participant was diagnosed with one or more treatable sleep disorders. These findings reinforce the necessity for routine screening for sleep disorders in persons with TBI. Moreover, when pharmacological management is prescribed for all sequelae of TBI, as well as other co-morbid health issues, it is essential to consider the possible effects of prescribed medications on sleep and wakefulness, both desirable and undesirable.

These results add to a small but growing body of evidence that sleep and wake disorders associated with TBI remain prevalent many years post-injury if left untreated. These disorders exacerbate trauma related cognitive, communication and mood impairments, and compromise outcomes. As such, there is a clear need for the systematic evaluation and treatment of sleep and wakefulness

4.6 Acknowledgements

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Chapter 5
Conclusions

Sleep is a universal physiological human need, occupying almost one third of the typical human life span. Sleep and sleep related disorders including disorders of wakefulness therefore, play an important role in relation to health and well-being. Sleep and wake disorders such as insomnia, and excessive daytime sleepiness affect large proportions of individuals with traumatic brain injury (TBI), across all levels of severity and across the continuum of recovery. Although they are among the most commonly reported neuropsychiatric sequelae following TBI, the impact of these disorders on aspects of rehabilitation and recovery, particularly, outcomes for cognition, communication, mood and participation, have received limited scientific attention until these current studies. Disturbances in sleep and wakefulness have been reported to exacerbate other trauma related disorders in cognition, communication, mood and pain, as well as compromise the rehabilitation process and community integration. It has been reported that 'sleep disturbance among persons with brain injury has a substantive negative impact on appraisals of quality of life; therefore, management of this problem is a major factor in the success of a posttraumatic rehabilitation program' (Mahmood et al., 2004, p. 379). Further it has been proposed that 'assessment and treatment of sleep disorders in patient management protocols improves clinical outcomes and reduces the persistence of cognitive, somatic, and emotional complaints among persons with brain injury' (Mahmood et al., 2004, p. 379), however, prior to this study, this had not been formally investigated. As such, the diagnosis and treatment of sleep and wake disorders associated with TBI has significant implications for participation in, and response to rehabilitation.

Thus, this doctoral thesis sought to answer the question regarding the nature and impact of TBI related sleep/wake disorders on aspects of recovery and outome. The overall objective was to gain a clear understanding of sleep and wake disorders after TBI and, to examine the impact of appropriate diagnosis and management on recovery

of cognition, communication and mood. To this end, three separate studies were conducted, including (1) An in-depth systematic review of the current literature regarding sleep and wake disorders following TBI, across 5 sub-topics including epidemiology, pathophysiology, neuropsychological implications, paediatrics and intervention, (2) A case study examination of a young adults with severe TBI, excessive daytime sleepiness and cognitive-communication impairments, and (3) then, to longitudinally and comprehensively examine cognitive, communication and mood outcomes in response to treatment for these disorders.

The label of TBI is one of the most challenging to categorize based on diagnosis, as it can result in a myriad of diverse and complex clinical presentations' (Wiseman-Hakes et al., 2010, p. 357). This was highly apparent throughout the course of this study, with the many different diagnoses and combinations of sleep and wake disorders, and the participants' unique presentation of cognitive, communication, physical, psycho-social impairments, and individual life circumstances.

5.1 Relevance of Thesis Findings to Rehabilitation from the Perspective of the International Classification of Functioning, Disability and Health (ICF)

What is also readily apparent throughout each component of this work, is that sleep and wake disorders impact across all domains and aspects of function, consistent with International Classification of Functioning, Disability and Health, and health-related domains; the ICF. These domains, classified from body, individual and societal perspectives by means of two lists: including a list of body functions and structure, and a list of domains of activity and participation. Since an individual's functioning and disability occurs in a context, the ICF also includes a list of environmental factors (WHO, 2002). In fact, there has been a recent trend towards examining health status measures in sleep medicine, and, problems of function in person with sleep disorders using the ICF (Gradinger, Glässel, Bentley, & Stucki, 2011; Gradinger, Glässel, Gugger, et al., 2011). A recently published systematic review by Gradinger, Glässel et al. (2011) examined and identified all of the measures used in sleep medicine, and the frequencies of ICF categories covering the concepts contained in the measures. Results revealed that of 115 patient-administered

measures, 4686 concepts contained in the items of all the sleep measures were linked to 133 different 2nd level ICF categories. Predominantly these were linked to 54 different ICF categories of the ICF component 'body functions' (61.4%), followed by 15.3% of concepts linked to 49 different categories of the component activities & participation, and 9.8% of concepts linked to 22 categories of the component environmental factors. The component body structures were the least frequent (0.5%). Of direct relevance to this current doctoral research, were their findings related to the categories:

(A) ***Body Functions****:* they identified that 88% of sleep measures had items related to the subheading *Sleep functions,* 57% had items related to the subheading *Energy and drive Functions,* 48 % of sleep measures had items related to the subheading *Emotional Functions,* 41 % of sleep measures had items related to the subheading *Temperament and personality functions,* and 30 % of sleep measures had items related to the subheading *Consciousness Functions.* These findings are particularly relevant for rehabilitation of individuals with TBI. All participants in the current study(s) had impairments in sleep, energy and drive (arousal and fatigue), temperament (which for purposes of this discussion is defined as emotional well-being) and consciousness functions such as difficulties with attention and processing of information, consistent with their diagnosis of TBI.

(B) ***Activities and Participation:*** 32% of sleep measures had items related to the subheading *Recreation and leisure,* 29% of sleep measures had items related to the subheading remunerative employment, 22% of sleep measures had items related to the subheading *Carrying out daily routine,* 19% of sleep measures had items related to the subheading *Maintaining a body position,* and 17% of sleep measures had items related to the subheading *Driving.* Again, this is highly relevant to TBI rehabilitation*.* All of the participants in the study(ies) had difficulties participating in recreation and leisure (in fact all participants reported that they rarely or never participated in recreation and leisure activities unless it was specifically part of a therapy, as they were too sleepy (or fatigued). Six participants were unable to work due to the impact of their sleep disorder, and as a result of treatment, 1 was able to return to work part-time, 1 was able to increase their

hours of employment, and 1 was able to begin the return to work process. All participants were compromised in regards to carrying out their daily routine by their sleepiness and or lack of energy. Four participants routinely fell asleep and were unable to maintain an upright body position at their clinical sleep appointments until treatment was optimized. All participants were either unable to drive, or their driving was compromised by their sleep disorder. Thus, the ICF provides a relevant and useful referent by which to further understand the impact of sleep disorders in this current study, and the implications of our findings globally to rehabilitation of persons with TBI.

Our results suggest that for these individuals to fully participate in and benefit from rehabilitation, adequate sleep and associated daytime arousal and wakefulness are required. It is therefore, of great importance that sleep and wakefulness be routinely assessed throughout the rehabilitation process, and that intervention(s) to optimize sleep and wakefulness be provided in collaboration with a team approach. Sleep and wakefulness education should also be incorporated into rehabilitation programs.

5.2 What This Thesis Adds to the Literature

In summary, our findings concur with previous studies in that sleep and wake disorders are a prevalent and complex sequelae of TBI occurring at all stages across the continuum of recovery from acute, to post-acute, to rehabilitation, in both children and adults, and for a number of patients, continuing for many years post-injury, long into the community if left untreated. These disorders are complex and multi-factorial, impact on neuropsychological and communication functioning, participation in rehabilitation and quality of life. An observable trend in increasing methodological quality and scientific rigor of the literature, has been observed as studies in the field are becoming more methodologically sound as the literature evolves. over time. The results of this thesis add considerably to the evolution of scientific investigation of sleep and wake disorders associated with TBI., We had similar findings regarding changes to sleep architecture, and we confirmed the importance and value of having self-report measures of sleep in addition to objective measures. Additionally, this body of work makes a number of novel and important contributions to the literature regarding sleep and wake disorders following TBI. Manuscript 1 is the first

systematic review on this topic, and, the first review to include literature on paediatrics, to identify practice points based on the evidence, identify gaps in the literature and a future research agenda. These findings drove in part, our methodologies for manuscripts 2 and 3. Manuscript 2 provides the first longitudinal study of cognitive, communication and mood outcomes as measured by self-report, in response to treatment for excessive daytime sleepiness in a young adult with severe TBI. It highlights the importance of self-report measure in determining response to intervention and outcome. It further highlights that these disorders evolve over time, as in this case, they became most prevalent at 1 year post-injury. It is also the first paper to report on the individualized approach to intervention for sleep and wake disorders in the TBI population, and how critical the successful management is with regards to participation in rehabilitation. Further, manuscript 2 introduces the Daily Cognitive Communication and Sleep Profile, DCCASP, a new measure designed to capture the perceived relationship between quality of sleep and wakefulness on daytime function in specific areas. This measure fills a gap in existing measures as it recognizes and thus compensates for memory difficulties typical of this population which may invalidate responses for other retrospective self-report measures. Manuscript Three builds on existing literature and provides the first comprehensive and longitudinal investigation of cognitive, communication and mood outcomes in response to treatment for sleep and wake disorders, in a sample of adults with chronic TBI. It further highlights that for the majority, these disorders do not 'resolve or just get better over time' if left untreated, and, it also emphasizes that individuals can still make gains in, or optimize cognitive, communication and mood function in response to treatment, even many years post-injury.

The findings of this research serve to highlight the relevance of the role of sleep in recovery, and the clear relationship between quality and quantity of sleep and cognition, communication and mood. The findings underscore the critical need for screening, systematic assessment and access to appropriate treatment for sleep and wake disorders for all those with TBI, across the continuum of recovery.

5.3 Future Research Directions

Further research is necessary to understand the evolution of sleep wake disorders after TBI, beginning right in the acute stage, and to understand the role of early sleep wake disorders on outcome. Imaging studies will also be of value in elucidating any structural changes related to alterations in sleep and wakefulness in those with TBI. There is also a need for future studies to examine sleep and wakefulness in the acute stages of TBI and to determine any relationships between resumption of a regular sleep wake cycle in the acute stage and neural recovery and outcomes. Based on the literature to date, it remains unclear exactly whom within the TBI population are at greatest risk for sleep and wake disorders, and, why there is such great variation in the types of sleep and wake disorders seen. Thus future studies should also examine who is at risk for each specific type of sleep disorder and the risk factors associated with each disorder, as well as for those whom fatigue, in and above sleep and wake disorders is a concern. Research is also needed to further elucidate how sleep/wake disorders evolves over time, and to determine methods for prevention of future sleep disorders. It remains unclear why those with mTBI and complicated mTBI are more likely to present with insomnia or symptoms of insomnia, and whether or not this is a true manifestation of the disorder, or a reflection of other issues such as greater self-awareness, the challenges of returning to work, school and community and such. Thus research is also needed to closely examine those with mTBI and determine the underlying factors contributing to or causing the prevalence of insomnia related disorders.

Another area that has not been formally investigated to date, and thus is warranted, is the role of sex and gender in the evolution of sleep and wake disorders. The confound of aging with a brain injury, including endocrine changes related to menopause in women and, other age related changes in sleep should also be examined.

What is needed is a large multi-centre study which follows all those with TBI from the acute stage with regular follow-up into the community, such that results can be reliable, valid and stratified by nature and severity of injury, age, sex, imaging results, and development of the disorder over time. Additionally, we recommend that outcomes for either epidemiological or intervention studies should also capture functional outcomes in

addition to sleep measures and cognitive measures to fully assess the impact of the intervention.

It is also important to study sleep and sleep wake disorders in children and youth with TBI from the perspectives of incidence, prevalence, risk factors, evolution of the disorder, implications for functional and neural recovery, and age appropriate) ideally nonpharmacological) interventions. In addition, considerable work needs to be done to identify effective interventions as well as management strategies for persons with sleep wake disorders associated with TBI.

Finally, we concur with Dr. Richard Castriotta in his 2008 editorial entitled *Collaboration in research involving traumatic brain injury and sleep disorders:*

> that "careful study will require much effort and many resources, which can best be brought to fruition through collaborative efforts across multiple centres, with an aim to elucidate the causes, foster early diagnosis, and develop optimal treatment for these problems". (p. 177)

These continuing efforts will further inform clinical practice and ultimately contribute to the development of practice guidelines for the systematic evaluation and treatment of sleep and wake disorders following TBI.

In conclusion, the findings of this body of work, from both a scientific perspective and functionally from a human perspective, greatly exceeded what was expected to be found at the onset of this process. On a personal note, I am even more convinced of the importance of this field of study, and critical role of sleep in recovery from TBI.

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Appendix A

Sleep and Wake Disorders Following Traumatic Brain Injury: Summary of Reviewed Articles

Reference	Study Objective	Research Design	Sample Size Inclusion/ Exclusion	Subjects	Data Collection Methods/ Measures	Significant Findings	Comments	Quality [a]
Epidemiology/Prevalence/Description: Comparison Group								
Fichtenberg et al., 2002 US	Type Epi/Prev/Desc Establish frequency of insomnia (diagnosis using DSM-IV) in TBI and compare it to insomnia rates in other rehab outpts	Level **III** Recruitment: Prospective cohort Consecutive OR Cross-sectional Comparison group (C): rehabilitation outpatients (same # spinal cord injury (SCI) and musculoskeletal (MSK))	TBI [b] =50 C=50: MSK=25; SCI=25 Inclusion: • Galveston Orientation and Amnesia Test (GOAT) > 75 • ≥ Rancho Los Amigos Level VI Exclusion: • not in PTA state	**Age:** (p<0.05) TBI 36.5±14.5 yrs; SCI 38.2±13.5; MSK 47.3±12.2 **Gender:** (p<0.05) TBI 44%F; SCI 24%F; MSK 80%F **GCS:** sTBI 42%; modTBI 18%; mTBI 40% **Time since:** 3.8±7.4 mos	PSQI BDI Sleep diaries (TBI only) Insomnia diag using DSM-IV criteria	TBI: ↓ sleep quality (initiation probs 2x duration probs); ↑ sleep duration TBI: 30 % insomnia diag (DSM-IV) TBI: ↓ PSQI global scores TBI: < insomnia rate than C	Prevalence of insomnia is 1/3 of TBI population First paper to use formal diagnosis of insomnia Limitations: Did not stratify results by severity Reliability of self-report sleep diaries	**Moderate:** 4.5/7 Baseline: 1 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Parcell et al., 2006 Australia	Type Epi/Prev/Desc Explore subj sleep reports from persons with TBI	Level **III** Recruitment: Consecutive PR (≥ 2 wks post d/c) Longitudinal Survey design C: general community, age and gender matched	TBI=63 C=63 Inclusion: • 16-65 yrs • facility in English • No transmeridian travel across > 1 time zone in previous 12 mos • No pre-inj sleep disorder • No benzodiazepines or other sleeping	**Age:** TBI 32.5±1.7 yrs; C 30.5±1.2 **Gender:** both grps 43% F **GCS:** 9.6±.57 PTA 19.8± 2.7: used for severity mTBI = 8; modTBI = 13; sTBI = 27; vsTBI = 14 **Time since:**	7-day self report sleep-wake diary (sleep and wake times, sleep onset latency, frequency, and duration of nocturnal awakenings and daytime naps) general sleep questionnaire to evaluate sleep changes and quality	TBI: > sleep changes; > night-time awakenings and longer sleep onset latency; more frequently reported by mTBI ↑ anx and dep assoc with↑ reporting of sleep changes	Strengths: Follow up and used a 7-day diary Considered other potential factors impacting sleep Limitations: Difference in time used to note changes (TBI 8 mos; C 3 mos)	**Moderate**: 4.5/7 Baseline: 1 Blinding: 0 Sample size: .5 Attrition: 0 Standardized outcomes:1 Description:

		TBI reflect on changes since inj and C reflect on changes in the last 3 mos Data collection: initial and 3 mos	medications • No previous BI, neurological disorder or major psychiatric disorder Screened by neuropsychologist to determine eligibility	mean 230 days	ESS HADS			1 Follow-up: 1
Watson et al., 2007 US	Type Epi/Prev/Desc Evaluate the prevalence of sleepiness following TBI	Level **III** Recruitment: Prospective cohort Consecutive A Longitudinal 2 Comparison grps; C1 non-cranial trauma admissions; C2 trauma free selected from friends of TBI Data collection: 1 mo and 1 yr post inj	TBI = 512 (N=346 @ 1 mo; N=410 @ 1yr) C1= 132 (N=131 @ 1 mo; N=124 @ 1yr) C2= 102 (N=101 @ 1 mo; N=88 @ 1yr) Inclusion: • Any period of LOC • PTA≥1hr • Other obj evidence of head trauma • Hospitalization ** some had pre-existing conditions: prior TBI, alcohol abuse, sig psychiatric disorder	**Age:** TBI 30±14yrs; C1 31.4±13.5; C2 24.5±8.1 **Gender:** TBI 27%F; C1 28%F; C2 56% F **GCS:** ≤ 10 at admission Inj severity: time from inj to a consistent GCS score of 6 **Time since:** 1 mos & 1 year at follow-up	Sickness Impact Profile (SIP): sleep and rest subscale consisting of 4 questions	TBI: 55% endorsed ≥1 sleepiness items 1 mo post inj vs C1 41% and C2 3% TBI: 27% endorsed ≥1 sleepiness items 1 yr post inj vs C1 23% and C2 1% TBI: sleepier than C1 at 1 mo but not 1 yr TBI are sleepier particularly those with more severe injuries; sleepiness ↓ in TBI but about 25% remain sleepy after 1 yr (also true for C1)	Strengths: Good follow up Limitations: Weak outcome measure; not separately validated; just descriptive data, large attrition Majority were mTBI as sTBI not able to complete the SIP; may lead to underestimate of the true sleepiness pattern in TBI	**Moderate**: 4.5/7 Baseline: 1 Blinding: 0 Sample Size: 1 Attrition: 0 Standardized outcomes: .5 Description: 1 Follow-up: 1
Beetar et al., 1996 US	Type: Epi/Prev/Desc Compare the incidence of sleep and pain in TBI and comparative neurologic populations	Level **III** Recruitment: OR (neuropsychology service) Cross sectional Case control	mTBI= 127 mod to sTBI = 75 C=123 Used Mild TBI Committee of the Head Injury Interdisciplinary Special Interest Group of the	**Age:** TBI 36.1±11.7; C 43.3±13.6 **Gender:** TBI 32%F; C 42% F **GCS:** NI **Time since:** TBI 23.9±2.2	Chart review Patient report of sleep and or pain problems	Sleep maintenance most common sleep problem TBI: 55% had insomnia complaints vs C < 33%	Strengths: One of earliest studies to document incidence Limitations: Retrospective and subj data collection	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 1

		study Consecutive chart review Comparison group: general neurologic pts referred for neuropsychological assessment	American Congress of Rehabilitation Medicine	mos (inj); C 35.5±23.3 mos (symptom)		TBI: > insomnia and pain complaints (2.5 x more); presence of pain ↑ insomnia report 2x TBI without pain: > sleep complaints than C and mTBI >mod/sTBI mTBI > pain than mod/sTBI Complaints ↓ with > time since inj		Attrition: 1 Standardized outcomes: 0 Description: 1 Follow-up: 0
Ouellet & Morin, 2006 Canada	Type: Epi/Prev/Desc: Compare subj and obj measures of sleep in TBI	Level **III** Recruitment: LC (rehabilitation centres and advertisements sent to TBI associations and support grps mailing lists) Cross sectional Comparison Group: healthy good sleepers matched on age and gender to TBI; recruited through advertisements and acquaintances of the authors 2 nights of PSG	TBI = 14 m to sTBI C = 14 Inclusion: • 18-50yrs • TBI ≤ last 5 yrs • Stable phys health • No longer an inpt • Have an insomnia syndrome Exclusion: • Major untreated or unstable co-morbid condition • Sleep difficulties before TBI • Evidence of another sleep disorder • Sig pain • Unable to complete the questionnaires	**Age:** TBI 30.4±9.7 yrs; C 30.0±10.0 **Gender:** 56% F **GCS:** 4 mild, 1 mild-mod, 4 mod, 3 mod-sev, 2 sev (criteria in article) **Time since:** 21 mos	Diagnostic Interview for Insomnia Sleep dairy PSG Sleep survey ISS MFI BDI Beck Anxiety Inventory	TBI: PSG showed 71% with insomnia Large effect sizes for total sleep time, wake after sleep onset, awakenings longer than 5 min, and sleep efficiency TBI: > proportion of stage 1 sleep When those using psychotropic meds excluded, TBI had > awakenings lasting longer than 5 min and a short REM sleep onset latency	Results similar to those with primary insomnia or insomnia related to depression Limitations: Small sample size and a lot of variability in TBI grp and presence of sleep problems in control grp Multiple comparison and lack of statistical power	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Parcell et al., 2008	Type Epi/Prev/Desc	Level **III**	TBI =10 C=10	**Age:** TBI 38.8±4.3;	Demographic and medication details	TBI: poorer sleep quality and higher	Documents importance of	**Moderate:** 4/7

Australia	Evaluate changes in sleep quality and changes in obj recorded sleep parameters after TBI and investigate the relationship between mood state and injury characteristics	Recruitment: AI (mod to sTBI) Cross sectional Survey and lab-based nocturnal PSG Comparison group: age- and gender-matched controls in general community PSG over 2 nights within 1 wk; evaluated in TBI and C pairs	Inclusion: • 16-65 yrs • English facility • Normal body mass index • No trans-meridian travel across > 1 time zone in previous 12 mo • No pre-inj sleep disorder • No benzodiazepines or other sleeping medications • No previous BI, neurological disorder or major psychiatric disorder	C 37.8 ±44.4 **Gender:** 40% F **GCS:** 10.9±1.0 40% mod TBI; 40% sTBI; 20% vsTBI PTA 16.44±4.3 days **Time since:** 516±124 days	at recruitment and inj details from medical records Sleep-wake diary for 7 days ESS Sleep quality questionnaire (TBI changes since inj and C changes in last 3 mos) PSQI Nocturnal PSG HADS	levels of anx and dep TBI: ↑ in deep (slow wave) sleep, ↓ in REM, > night-time awakenings TBI: > anx and dep which co-varied with the observed sleep changes	subj report as central to diag and treatment but need to consider obj data as well Provides many important practice points; is a strong contributor to clinical and research literature	Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Schreiber et al., 2008 Israel	Type Epi/Prev/Desc: Identify the characteristics of sleep disturbance in adults after mTBI	Level **III** Recruitment: Retrospective Consecutive OR (where sleep lab data available) Cross sectional Comparison Group: matched and referred for sleep evaluation as part of routine pre-employment assessment TBI 2 nights PSG (not on a weekend); C only 1 night MSLT on day between the 2 nights	mTBI = 26 C=20 (apparently healthy) Inclusion: • 21-50 yrs • Documented (≥ 1 yr since mTBI • Normal brain CT, MRI • Negative electroencephalogram (EEG) • No past history of CNS pathology • No pre-morbid or present major psychiatric diag • No sleep apnea or restless legs syndrome	**Age:** TBI 31.6±8.8 yrs; C 33.8±7.8 **Gender:** NI **GCS:** NI **Time since:** 12 mos to 21 yrs	PSG MSLT	TBI: sleep patterns disturbed; sleep architecture altered: < REM sleep scores and > NREM scores TBI: MSLT documented sig EDS	Important to identity those who need treatment for sleep problems Limitations: C were not all within the normal values Possible issues of recall bias Wide range of time post inj Difference in data collection strategy between the two grps	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

Williams et al., 2008 Canada	Type: Epi/Prev/Desc Characterize the extent and nature of disrupted sleep in individuals with long-term sleep complaints subsequent to mTBI (i.e., sport-related concussion) To determine whether sleep disturbances in mTBI are more characteristic of psychological, psychiatric, or idiopathic insomnia	Level **III** Recruitment: LC (university setting) Cross sectional Comparison Group Face-to-face interview and laboratory PSG	TBI = 9 C = 9 Inclusion: • 18-26 yrs TBI: • Between 6 mos and 6 yrs post-inj • symptoms of Post Concussion Syndrome (PCS) at the time of inj • clearly distinguish between sleep patterns before and after inj • sleep difficulties within 1 mo of inj • sleep complaints characterized by sleep onset of > 30 mins on ≥ 4 or days in a wk C: • no previous BI • No sleep difficulties	**Age:** TBI 21.4±2.4; C 20.7±2.1 **Gender:** TBI 33%F; C 56% F **GCS:** mild range; LOC for ≤ 5 minutes **Time since:** TBI 27.8 ±15.5 mos	Personality Assessment Inventory (PAI): dep and anx Brock Adaptive Functioning Questionnaire (BAFQ) PSQI Sleep Disorders Questionnaire (SDQ) Brock sleep and insomnia questionnaire Sleep log for 2 wks PSG for 3 consecutive nights Power spectral (FFT) analysis of the sleep onset period	TBI: long-term trouble with initiating/ maintaining sleep with attention and memory and affective (dep and anx) abnormalities; sig diff shown in PAI, BAFQ, PSQI TBI: 4% less efficient sleep, shorter REM onset latencies, longer sleep onset latencies (variability within sample); FFT revealed greater intra-subject variability in sigma, theta and delta power during sleep onset TBI different from C but not easily classified into existing insomnia subtypes	Sleep disturbances can persist well after injury Strengths: Very thorough study Limitations: Small N, sample of convenience (student volunteers) Confirmation of subj self-reports with PSG Highlights need to look at sport-related concussion	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Gosselin et al., 2009 Canada	Type: Epi/Prev/Desc Investigate the effects of sport-related concussion on subj and obj sleep quality	Level **III** Recruitment: LC (independent of the nature of reported symptoms) Cross sectional Used concussion diagnostic criteria	ABI = 10 C = 11 Inclusion: • ABI: history of at least 2 concussions Exclusion: • Presence of neurological or psychiatric diseases	**Age:** ABI 24.3 ± 6.1 yrs; C 22.6 ± 2.4 **Gender:** ABI 30%F; C 34% F **GCS:** ABI all 13-15 # concussions: 4.6±2.1 with at least 1 in last	PSG QEEQ: assessment of 10-min period of wakefulness 30-mins after sleep offset Post Concussion Symptom Scale (PCSS) PSQI ESS BDI	ABI: >symptoms, worse sleep quality; > delta activity and < alpha activity during wakefulness Concussion seems to be associated with a wakefulness problem rather than sleep	Discrepancy between subj and obj findings; not explained by depression nor hyper arousal Limitations: Small sample and with exclusions the sample became even smaller however,	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1

		Comparison group: No history of concussion; matched on age, gender, education and age started playing the sport PSG on 2 consecutive nights in the lab	• Extremely early or late habitual bed times • Use of drugs known to affect sleep or daytime sleepiness • Work the night shift • Travel to another time zone in last 2 mos	yr **Time since:** NI	Local developed questionnaire on sleep quality Cog Sport computer battery: short neuropsychology evaluation adapted from National Football League battery	disturbance Athletes with worse sleep quality (PSQI) and symptoms (PCSS) > relative delta power during daytime; ABI lower PSQI associated with ↓ in REM sleep efficiency PSQI and PCSS correlated Absolute spectral power showed high inter-subject variation in ABI therefore analyze on the relative spectral power	highlights need to assess sleep and wakefulness following sport-related concussion Only a pilot study	Description: 1 Follow-up: 0
Reference	**Study Objective**	**Research Design**	**Sample Size Inclusion/ Exclusion**	**Subjects**	**Data Collection Methods/ Measures**	**Significant Findings**	**Comments**	**Quality**
Epidemiology / Prevalence/Description: Cohort/Single Group								
Baumann et al., 2007 Switzerland	Type: Epi/Prev/Desc Determine the frequency and clinical characteristics of post-traumatic sleep-wake disorder (SWD); assess cerebral spinal fluid (CSF) hypocretin levels 6 mos after TBI and risk factors for post traumatic SWD.	**Level III** Recruitment: Prospective study Consecutive A (within 4 days of inj) Longitudinal Single Group Baseline: laboratory tests 6 mo: other outcomes,	TBI= 65 (96 enrolled; 76 available for follow-up) Inclusion: • acute, first ever TBI Exclusion: • sleep-wake or psychiatric disorders diagnosed prior to TBI	**Age:** 16-72, mean 38± 16 yrs **Gender:** 14% F **GCS:** mean 10.2, mTBI: 40%; modTBI: 23%; sTBI: 37% **Time since:** 6 mos after TBI	CT scan CSF hypocretin-1 levels Human leukocyte antigen (HLA) typing Interview: social status and residual symptoms post inj, including sleep habits Neurological examination using a standard protocol, with the Folstein Mini	SWD are common after TBI, EDS/fatigue = 55% Post traumatic hypersomnia = 22% Low hypocretin levels found in 19% 6 mos after inj vs 93% in first days after inj 6 mo hypocretin levels were lower in those with post traumatic SWD	Strengths: Very thorough Limitations: Attrition was large and not all available for laboratory follow up	**High:** 5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 0.5 Standardized outcomes: 1 Description: 1 Follow-up: 1

		subsample repeated laboratory tests			Mental Status Examination (MMSE) BDI Medical Outcomes Study Short Form – 36 ESS Sleep Apnea Scale of the Sleep Disorders Questionnaire Ullanlinna Narcolepsy Scale Swiss Narcolepsy Scale PSG MSLT Actigraphy.	No other sig relationships were found Hypocretin system possible contributor to pathophysiology of post traumatic SWD		
Castriotta et al., 2007 USA	Type Epi/Prev/Desc Determine the prevalence and consequences of sleepiness and sleep disorders after TBI Explore relationship between presence of sleep disorders, inj characteristics and subject variables	**Level IV A** Recruitment: Prospective study AI (3 centres) Single Group Cross sectional	TBI=87 Inclusion: • > 18 yrs old • ≥ 3 mos post inj Exclusion: • presence of circadian rhythm disorder • use of sedating medications • unable to give informed consent	**Age:** 38.3± 15.1 **Gender:** 28% F **GCS:** NI Severity: Mild 8%, moderate 175, moderate-severe 6%, severe 33%, unknown 36% **Time since:** 64.3±117.7 mos	PSG MSLT ESS Psychomotor Vigilance Test (PVT) Profile of Mood States (POMS) Functional Outcome of Sleep Questionnaire (FOSQ)	23% OSA 46% Abnormal sleep studies 11% post traumatic hypersomnia 6% narcolepsy 7% periodic limb movements 25% with obj EDS No correlation between ESS and MSLT(r=0.10) No differences in demographics and inj chars between sleepy (Sl) and non-sleepy (NSl) Ss BMI: Sl >NSl PVT: Sl<NSl FOSQ: Sl better NSl POMS: no differences	Strengths: First study to show that a sleep disorder adds an additional cognitive burden Limitations: No obj measure of daily functioning	**High:** 5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

Fichtenberg et al., 2000 USA	Type: Epi/Prev/Desc Relationship between insomnia and demographics, injury and psychological variables in post-acute TBI	Level IV A Recruitment: Prospective study Consecutive OR Cross sectional Single Group	TBI=91 Inclusion: • diag of TBI on basis of examination • recovery to post-acute phase • medical determination of need for outpt neurorehabilita-tion Exclusion: • in state of PTA • rated below Level VI on Levels of Cognitive Functioning Scale (LCFS) • using sleep medication	**Age:** 33.8± 14.5 yrs **Gender:** 41% F **GCS**: 13-15: 33% 9-12: 21% 3-8: 46% **Time since**: mean 3.3 mos	PSQI BDI GOAT LCFS	Strong relationship between insomnia and depression. Pain disturbance of sleep was sig associated with insomnia. BDI : 68% depressed were suffering with insomnia	Strengths: Identifies a developmental pattern that may progress from a physiological basis to a secondary disorder associated with depression	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Ouellet, Beaulieu-Bonneau, & Morin, 2006 Canada	Type: Epi/Prev/Desc To determine the frequency of insomnia according to DSM-IV and International Classification of Sleep Disorders (ICSD) criteria. To describe clinical and socio-demographic characteristics of insomnia in TBI	**Level IVA** Recruitment: LC (French-speaking from rehabilitation centre archives and on mailing lists of TBI associations in Quebec) Mailed questionnaire Cross sectional Single Group Significant others completed a brief parallel evaluation	TBI=452 Inclusion: • ≥16 yrs • TBI: minor, mild, moderate or severe	**Age:** 40.2 ±13.1 yrs **Gender:** 35% F **GCS:** NI Severity: 59.9% sTBI 23.3% modTBI 13.7% mTBI (criteria includes GCS) **Time since:** mean 7.8 yrs	Questionnaire booklet entitled "Quality of sleep and level of fatigue following a TBI": Locally developed questions ISS Multi dimensional fatigue inventory Indice de détresse psychologique de L'Enquête Santé Québec (French adaptation of Psychiatric Symptom Index) Significant Other's Evaluation Questionnaire (significant other versions of ISS and other above	Insomnia prevalent after TBI, 64.3% with sleep onset insomnia, 76.6% with sleep maintenance insomnia Predictors of insomnia: lesser severity of BI, depressive symptoms, self-reported pain, fatigue	Limitations: Only subj data Under-representation of mTBI Those with insomnia problems may have been more motivated to respond Not able to determine insomnia subtypes	**Moderate:** 4.5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 0.5 Description: 1 Follow-up: 0

					questions)			
Rao, et al., 2008 USA	Type: Epi/Prev/Desc To assess the prevalence of and risk factors for sleep disturbances in acute post-traumatic TBI	**Level III** Recruitment: PAC (within 3 mos of trauma) Longitudinal observational study Single Group Data collection: 1. within 2 wks of inj to assess history of psychiatric and sleep problems; 2. within 1-3 mos of inj; for some both at the same time	TBI=54 Inclusion: • ≥18yrs • able to provide informed consent • admitted to hospital with experience of LOC • GCS ≤ 15 • Positive CT findings Exclusion: • prior TBI • open head injury • history of other type of illness	**Age:** 43.2± 17.7 yrs **Gender:** 41% F **GCS:** mean 12.5± 3.6 65% mild, 11% moderate, 19% severe **Time since:** ≥ 3 mos	Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID-IV) General Medical Health Rating Scale (GMHR) MOS Self-report for anx and dep	Worse on most sleep measures after TBI compared to before TBI Anx disorder secondary to TBI was most consistent sig risk factor to be associated with worsening sleep status	Strengths: Assesses sleep problems in the acute period Participants had a range of severities Limitations: Subj data and recall bias might be an issue Lack of info on other potential influencing factors (pain, medical problems, and medications)	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0.5
Clinchot et al., 1998 USA	Type: Epi/Prev/Desc Define and correlate the incidence and type of sleep disturbances that occur after BI	**Level V** Recruitment: Prospective study Consecutive AI Single Group Longitudinal Baseline and 1 yr follow up post d/c via telephone interview	TBI=145 Inclusion: • ≥14 yrs with sustained BI Exclusion: • Not acute inj • Primarily the result of anoxia	**Age:** 31 yrs **Gender:** 23% F **GCS:** median=4 **Time since:** mean 20 days	Direct observation Medical Record extractions Agitated Behaviour Scale FIM Wechsler Memory Scale (WMS) Halstead Reitan Neuropsychological Battery Follow up interview: Community Integration Questionnaire Sleep difficulties, medical problems, medications, services used	50% diff with sleep, 25% sleeping more and 45% diff falling sleep GCS≤ 7 less likely to have problems with sleep than GCS>7 64% with sleep diff waking up too early Sleep complaints correlated with presence of fatigue, > GCS, better immediate memory, positive substance abuse history, > age,	Limitation: Large number lost to follow up; those lost more likely to have a history of substance abuse Self-report of sleep difficulties	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 0 Standardized outcomes: 1 Description: .5 Follow-up: 1

						and being female		
Webster et al., 2001 USA	Type Epi/Prev/Desc Determine the occurrence and nature of sleep related breathing disorders in adults with TBI	**Level IV A** Recruitment: Prospective observational study Consecutive AI Single Group	TBI=28 Inclusion: • 18-65 yrs • < 3 mos post inj • Rancho ≥ 3 Exclusion: • Previously documented sleep apnea, narcolepsy, or habitual snoring • Tracheostomy • History of other premorbid neurologic or pulmonary conditions	**Age:** 34.5 yrs **Gender:** 25% F **GCS:** lowest during the first 24 hrs; 71% GCS≤8 25% GCS 9-12 4% GCS >12 PTA >1 day Rancho 95% Level VI or VII **Time since**: < 3 mos	Overnight sleep study using portable 6-channel monitoring system; calculated a respiratory disturbance index (RDI)	Sleep related breathing disorders defined by a respiratory index of 5 or greater appears to be common in adult subjects with TBI. Evidence of sleep apnea was found in 36% of subjects.	Strengths: Prospective and consecutive design New info regarding the occurrence of sleep apnea in early recovery phase Attempt to eliminate confounding factors Limitations: Low power Homogeneous sample Not able to collect EEG data	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0.5 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Masel et al., 2001 USA	Type Epi/Prev/Desc Determine prevalence, demographics and causes of EDS in adults with BI and investigate relationship between subj and obj data	**Level III** Recruitment: Consecutive AI Case series Cross sectional Single Group 2 overnight sleep evaluations 1 wk apart; actigraphy for 2 wks after 2nd PSG	TBI=71 Complete medical history and physical examination Inclusion: None Exclusion: None	**Age:** 32±11 yrs **Gender:** 38% F **GCS:** only for 56%: Non hypersomnia (NH) 6±4; Post traumatic hypersomnia. (PTH) 7±5; Hypersomnia with abnormal indices (HAI) 8±5 Rancho ≥ Lev IV **Time since:** 38±60 mos	Actigraphy PSG MSLT ESS PSQI Millon Clinical Multiaxial Inventory - II (MCMI-II) Neuropsychologic battery Diag of narcolepsy and post traumatic hypersomnia using the ICSD	Hypersomnia was common with high presence of sleep apnea hypopnea syndrome, periodic limb movements and PTH NH: N=38; PTH: N=21; HAI: N=12 No relationship between hypersomnia grps and GCS, psychopathology, time post inj, and demographic variables; no sig differences of note on the	Suggest maybe that TBI have an inability to perceive their hypersomnolence Limitation: Wide range of time post inj Self-selection bias	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

						neurologic tests No sig correlation between ESS or PSQI and MSLT		
Verma et al., 2007 USA	Type Epi/Prev/Desc Determine the spectrum of sleep disorders in pts with chronic TBI and determine if the severity of sleep disorder is related to severity of chronic TBI.	**Level V** Recruitment: Retrospective LC (Referred for evaluation for sleep disorder) Cross sectional Single Group One overnight PSG	TBI=60 Inclusion: NI Exclusion: NI	**Age:** 20-69 yrs, mean 41 yrs. **Gender:** 37% F **GCS:** NI Severity assessed by GAF: mild 40% moderate 20% severe 40% **Time since:** 3mos-2 yrs	Detailed medical history, neurological exam, neck size, chin size and position, jaw alignment, and oropharyngeal examination PSG MSLT ESS BDI Hamilton Anxiety Scale	A full spectrum of sleep disorders occur in patients with chronic TBI Complicated relationship with severity of inj EDS was most common presenting symptom; which may lead to other problems like insomnia, anx and dep	Strengths: Identifies and describes the spectrum of sleep disorders Sleep disturbances can compromise rehab process and return to work Limitations: Retrospective 1 night of PSG Lack of exclusion of possible effects of meds and pain HAS and BDI not collected on all participants GAF may not be best evaluation of severity	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Castriotta & Lai, 2001 USA	Type Epi/Prev/Desc Determine the frequency of sleep disorders associated with TBI; investigate relationship between post	**Level III** Recruitment: Prospective cohort study Consecutive yet timing post inj unclear Cross sectional	TBI=10 Inclusion: • subj excessive sleep • ≥ 18 yrs or older • alert and oriented Exclusion: • medications to	**Age:** 56.3± 5.3 yrs **Gender:** 60% F **GCS:** sTBI 60%, mTBI 40% **Time since:** ≥72 hrs; 110±191 mos	Clinical interview ESS PSG MSLT	Sleep disordered breathing was found in 7 subjects Overt OSA in 5 subjects Narcolpesy in 2 subjects	Strengths: Prospective Limitations: Small sample	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1

	traumatic sleep disorders and pre-traumatic sleep disorders.	Single Group Use criterion standard to diag sleep disorders Those with overt sleep apnea had a 2nd PSG with titration of nasal continuous positive airway pressure	cause hypersomnolence • pregnancy • pts with cardiopulmonary and recent abdominal and thoracic injuries			Treatable sleep disorders appear to be common in sleepy TBI population All 10 had treatable sleep disorders; 3 had symptoms of hypersomnia before inj		Standardized outcomes: 1 Description: 1 Follow-up: 0
Chaput, 2009 Canada	Type: Epi/Prev/Desc Assess the relationships among sleep complaints, headaches, and mood alteration in mTBI	**Level III** Recruitment: Retrospective chart review Consecutive ER Single Group Longitudinal Data retrieval at 10 days and 6 wks Self report: in order to prevent selection bias those pts assessed by self-report and history were not excluded but rated for presence or absence of 6 types of sleep complaints	TBI=443 @ 10 days 87.8% @ 6 weeks 64.1% Inclusion: • Seen for ≥ 1 visit where post-inj symptoms not due to alcohol or other illegal substance, or medication, or other injuries or 2° to treatment of other inj • mTBI diag by neurosurgeon based on task force criteria Exclusion: • ≤ 16 yrs • language barrier known history of mental retardation, diag of dementia or learning disability impairing the cognitive and reasoning process, or co-existing psychiatric illness	**Age:** mean 46.9 yrs **Gender:** 31.8% F **Severity:** mTBI **GCS:** scene: mean 13.2 (10 day grp) and 15 (6 wk grp) Emergency department: 13.9 and 15 42% abnormal CT-scan **Time since:** <10 days post-trauma and < 6 wks	Review of past medical history including current medications, known allergies as well as smoking, alcohol and drug intake habits CT scans were reviewed if present Rivermead post-concussion symptom assessment questionnaire	Sleep complaint prevalence: 13.3% and 33.5% (sig more likely at 6 wks) Presence of sleep complaints is sig associated with headaches, depressive symptoms and feeling irritable at 10 days and 6 wks Early development of symptoms may increase risk of chronicity of symptoms Appear to indicate an alteration in sleep homeostasis following mTBI despite absence of physical pain as presented at 10 days	Limitations: Did not assess current stressors Subjective nature of data collected	**Moderate:** 3.5 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 0 Standardized outcomes: 0.5 Description: .5 Follow-up: 1

Makley, 2009 USA	Type: Epi/Prev/Desc Investigate whether improvements in sleep efficiency correlate with duration of PTA after closed head injury (CHI)	**Level IVA** Recruitment: Prospective Consecutive AI Single Group Longitudinal Actigraphy within 72 hrs of admission and for duration of stay (min of 7 days) Daily measurement of PTA; cleared when O-LOG score of ≥25 on 2 consecutive days Follow-up at 3 mo	CHI=14 Exclusion: • known history of a sleep disorder, anoxic injury, active psychiatric illness, obesity, untreated thyroid disease, degenerative neurologic condition, sig tetraparesis or immobility	**Age:** 24-45 yrs **Gender**: NI **GCS:** NI **Time since:** 15 days (9-23)	Complete neurologic and physical examination on admission FIM at admission and d/c Actigraphy The Orientation Log (O-LOG) to measure PTA by SLPs blinded to sleep scores Bedside sleep logs kept by nursing staff Follow-up: DRS Supervision Rating Scale SWLS PSQI	78% had mean Week-1 sleep efficiency in the severely impaired range Those admitted having already cleared PTA had sig better Week-1 sleep efficiency than those with ongoing amnesia Those with ongoing amnesia: each 10-unit inc in sleep efficiency correlated with 1 unit ↑ in O-LOG score Association between improvement in sleep efficiency and return of awareness > for those admitted with PTA	Actigraphy a good method to measure sleep patterns in immediate post-acute Strengths: Effort made to measure/eliminate potential confounding variables Limitations: Small sample with large attrition (only 9 available for analysis)	**Moderate:** 3.5 Baseline: 0.5 Blinding: 0.5 Sample size: 0 Attrition: 0 Standardized outcomes: 0.5 Description: 1 Follow-up: 1
Worthington & Melia, 2006 UK	Type Epi/Prev/Desc Investigate the impact of disorders of arousal and sleep disturbance on everyday living and participation in rehabilitation.	**Level V** Recruitment: Retrospective naturalistic observation Recruitment AI (7 centres Cross sectional Single Group	ABI=135 Inclusion: • admission to service on grounds of sig cognitive and/or behaviour disorder • severe BI • all able to participate in rehab Exclusion: NI	**Age:** 38± 11.4 yrs **Gender:** 25% F **GCS:** ranged from 3-7 **Time since:** 119.3± 108.8 mos	Structured rating form: 5 key features - delayed sleep onset, frequent waking at night, early morning waking, delayed morning waking, EDS	47% disturbance of arousal and sleep patterns; Sig adverse effect on activity in 66% of 47% Disordered arousal could persist up to 10 yrs post-inj Concurrent psychiatric illness, but not epilepsy, was associated with arousal and	Strengths: 1st sizeable study to address the impact and management of arousal disorders after BI	**Moderate:** 3/7 Baseline: 0.5 Blinding: 0 Sample size:1 Attrition: 1 Standardized outcomes: 0 Description: .5

						sleep disorder Non-pharmacological interventions used in 34% of cases; benzodiazepine/ hypnotic drugs 20% Long term outcome from sBI affected by enduring disturbance of arousal, most commonly noted as sleep disorder		Follow-up: 0
Reference	**Study Objective**	**Research Design**	**Sample Size Inclusion/ Exclusion**	**Subjects**	**Data Collection Methods/ Measures**	**Significant Findings**	**Comments**	**Quality**
Pathophysiology								
Ayalon et al., 2007 US	Type Pathophysiology Describe the physiologic and behavioural characteristics of circadian rhythm sleep disorders (CRSD) following mTBI in pts complaining of insomnia	Level **III** Recruitment: LC Descriptive Cohort Cross sectional Data collection every 2 hrs for 24 hrs	TBI=42	**Age: m**ean 26 yrs (17-45 yrs) **Gender:** 20% F **GCS:** mTBI **Time since:** NI	Actigraphy Saliva melatonin Oral temperature PSG Self report questionnaire to determine circadian preference: morningness-eveningness questionnaire	36% had CRSD 19% had DSPS: showed ↑temp, rhythm, amplitude 17% had irregular sleep-wake pattern (ISWP): had weaker circadian rhythmicity – account for behaviour differences in sleep-wake pattern? Distinct profiles of 24-hr periodicity of melatonin rhythm and 24-hr periodicity of oral temperature	mTBI might contribute to emergence of CRSD Important to have correct diag or can inappropriately treat for insomnia	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

Baumann et al., 2005 Switzerland	Type Pathophysiology Assess the CSF hypocretin-1 levels in pts with TBI	Level **III** Recruitment: Consecutive A Cohort Cross sectional Data collection 1-4 days post TBI	TBI = 44 C= 20 (no neurologic problems) Inclusion: • Acute TBI, 1-4 days post inj Exclusion: NI	**Age:** mean 36 yrs (17-69 yrs) **Gender:** 73% F **GCS:** 31 sTBI; 8 mod TBI; 5 mTBI **Time since:** 1-4 days	TBI:Hypocretin-1 levels assessed ventricular CSF (N=37) and spinal CSF (N=8) by radioimmunoassay C: levels assessed via spinal anaesthesia and some ventricular Used Marshall to categorize the CT	Hypocretin-1 levels abnormally low in 95% of mod-s TBI and in 97% of those with post-traumatic brain CT changes Site of CSF sample not matter Marshall I: 8; II-IV: 36 N=9 concomitant diseases	Change in levels may reflect hypothalamic damage and may be linked to SWD May also reflect loss of consciousness Limitations: Small sample size	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Quinto et al., 2000 US	Type Pathophysiology Describe the experience of Delayed Sleep Phase Syndrome (DSPS) in ABI	**Level IVA** Recruitment: LC Single Subject Case Study	TBI = 1 Sleep onset insomnia: not responsive to pharmacological treatment	**Age:** 48 yrs **Gender:** male **GCS**: NI **Time since:** NI	Sleep logs Actigraphy	Sleep onset insomnia with frequent awakenings Chronotherapy unsuccessful declined Phototherapy declined	Authors hypothesize lesion to suprachiasmatic nucleus (SCN) which is the site of human circadian clock Emphasized need to be aware of DSPS as a potential consequence of ABI when diagnosing sleep problems	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

Reference	Study Objective	Research Design	Sample Size Inclusion/ Exclusion	Subjects	Data Collection Methods/ Measures	Significant Findings	Comments	Quality
Paediatric								
Beebe et al., 2007 US	Type Paediatric Determine the effect of mod and severe TBI on sleep of school-aged children	**Level III** Recruitment: Concurrent prospective cohort A (children aged 6-12 yrs) Longitudinal 3 grps: modTBI, sTBI, orthopaedic inj Baseline (Retrospective parental report of pre-inj sleep at 3 wks post), 6, 12, and 48 mos post-inj	mod TBI = 56 sTBI = 53 C= 80 Inclusion: • 1 night in hospital for all 3 grps • No evidence of abuse or previous neurological disorder • English-speaking	**Age:** @ inj 9.5±2.0 yrs **Gender:** 33% F **GCS:** used lowest post-resuscitation/ inj score **Time since:** 3 wks post **Other:** 68% Caucasian	Child Behaviour Checklist: 7 items only (assessed stability in comparison to full scale)	mod TBI worse pre-injury sleep mod TBI and C: small ↓ in sleep from pre to post sTBI: ↑ in post-injury problems: daytime sleepiness and nocturnal sleep duration	Limitations: Timing of follow ups varied Retrospective data collection Weak instrument (only 7 items and part of larger scale)	**Moderate:** 4.5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 0 Standardized outcomes: 0.5 Description: 1 Follow-up: 1
Kaufman et al., 2001 Israel	Type Paediatric Subj and obj characterize the long term effects of mild head injury (mHI) on sleep in adolescents	**Level III** Recruitment: Prospective cohort A(archives) Cross sectional mHI: subj and obj measures C1, C2: obj only C1, C2 matched for age, gender; recruited by advertisement, word of mouth	mHI = 19 C1 (healthy) = 16 C2 (healthy) = 15 Inclusion: • 10-18 yrs • Hospital admission with mHI (ICD-10 codes) • GCS≥13 • 3 yrs post inj • Complained of sleep disturbance Exclusion: NI	**Age:** 13.5 ± 1.7 **Gender**: mHI 21%F; C1 19%F C2 20%F **GCS:** ≥13 **Time since:** 3 yrs post inj	Locally developed questionnaire: medical history, details of the inj, sleep habits, and sleep disturbances: pre and post sleep PSG (mHI and C1): 1 night Actigraphy (mHI and C2): 5 days within 3 mo of PSG	mHI: sig ↓ in sleep period time, total sleep time and sleep efficiency mHI: sig ↑ mins awake and number of awakenings > 3 mins mHI: subj report difficulty falling asleep, difficulty waking in the morning, daytime sleepiness, restless sleep,	Strengths: Thorough evaluation Use of healthy controls Subj corroborated obj for the most part Participants 3 yrs post inj so identifies/confirms long term sleep problems Limitations: Small N but reflective of the realities of this type of research	**Moderate:** 3.5/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: .5 Description: 1 Follow-up: 0

		One data collection, including 5 days of actigraphy				fearful wakenings from sleep, parasomnias		
Milroy et al., 2007 UK	Type Paediatric Obtain obj and subj reports of sleep disturbances in school-aged children with mTBI	**Level III** Recruitment: A (from database) Cross sectional 2 grps: mTBI and orthopaedic controls with inj to wrist or arm	mTBI = 18 (43% of admissions) C = 30 (61% of admissions) Inclusion: • 7-12 yrs • ≥ 6 mos since last hospital attendance • Admission < 48 hrs Exclusion: • Developmental delay, epilepsy, psychiatric, or sleep disorders • Attends a special school • Other recent hospitalization • History of non-accidental inj •	**Age:** mean TBI:9.7±1.5 yrs; C: 9.7±1.5 yrs **Gender:** TBI 56%F, C 40% F **GCS:** GCS of 15 = 16 GCS of 13 = 1 GCS of 14 =1 2% recorded PTA **Time since:** mean TBI 23.9 mos; C 25 mos	Actigraphy for 5 nights Parental and self report questionnaires: Children's Sleep Habits Self-Report Sleep Scale Strengths and Difficulties Demographic and injury-related questions	mTBI: Parents report > sleep disturbances when compared to C (medium effect size) mTBI and C: did not differ on measures of sleep efficiency	Higher proportion in both grps with sleep difficulties than expected Differences between parental report and obj measures of interest as these measures serve different purposes and may identify different types of sleep difficulties Self selection bias possible	**Moderate**: 4/7 Baseline:1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Necajauskaite et al., 2005 Lithuania	Type Paediatric Investigate the clinical features and prevalence of symptoms of PCS in children with mTBI and evaluate changes over time	**Level III** Recruitment: A Cross sectional Two grps: TBI: single mTBI; C: mild body injury 2 questionnaires mailed separately: 1st for period during	TBI= 102 C = 102 Grps matched on gender, age, date of admission	**Age:** 4-16 yrs **Gender:** 28% F **GCS:** NI **Time since:** 1-5 yrs post admission	Locally develop standardized questionnaire addressing: health and symptoms (irritability, fears, sleep disorders, learning problems, concentration problems, memory disorders, headaches and concomitant symptoms prior to trauma)	16.7% of parents reported sleep problems shortly after head trauma	Limitations: Criteria measured here not reliable estimates of long-lasting PCS Weak measures Only 1 data collection from C Retrospective; possible issues of recall bias	**Moderate:** 3.5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 0 Description: .5

		the last yr and during the last mo with no ref to trauma (to reduce bias); 2nd (just TBI grp) for period shortly after the trauma Compared those <2 yrs post inj to those 2-5 yrs post inj						Follow-up: 0
Korinthenberg et al., 2004 Germany	Type: Paediatric Investigate predictive factors of post traumatic syndrome in children with mHI	**Level III** Recruitment Prospective cohort Consecutive A (used specific criteria) Longitudinal Obj and subj measures Data collection: baseline and follow up at 4-6 wks	mHI= 98 Inclusion: • LOC < 10 or none • Able to answer questions at admission • No complications, confusion, or intracranial haemorrhage • Age 3-13 yrs • Child and parents speak German, parent available for interview Exclusion: NI	**Age:** 3-5 yrs=26, 6-9=42, 10-13=30 **Gender:** 40% F **GCS:** NI **Time since:** < 24 hr since admission	EEG Protocol of "examination of child with minor neurological dysfunction" Structured validated interview	At follow up: 23% presented with somatic and psychiatric complaints including sleep disturbance and fatigue, which did not correlate with somatic, neurologic or EEG findings immediately post-inj	Strengths: Large sample size Thorough investigation with follow up Limitations: Better with a further follow up	**Moderate:** 5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0.5
Pillar et al., 2003 Israel	Type: Paediatric Assess the prevalence and risk factors of long term sleep disturbances in adolescents after mHI	**Level III** Recruitment: Retrospective cohort A ("random" selection from archives) Cross sectional Matched controlled	mHI=98 C=80 Inclusion: • 7-15 yrs at inj • Admitted to hospital with mHI • ICD-10 codes 506.0 • GCS ≥13 on admission et ER Exclusion: NI	**Age:** 8-18; 13.5±2.3 yrs **Gender:** 32% F **GCS:** 14.7±0.6 on admission **Time since:** 0.5-6 yrs	Detailed 60-item questionnaire	mHI: 28% had sleep problems (vs C 11% - p<0.05) mHI > C: average score of sleep complaints (p<0.05) mHI with sleep complaints (N=27) had > body	Strengths: Large sample size Comprehensive questionnaire Large range post-inj Comparison group Limitations: 2/3 response rate	**Low:** 2.5/7 Baseline: 1 Blinding: 0 Sample size:1 Attrition: 0 Standardized outcomes: 0

		comparison group (healthy)				weight, > BMI, parents less educated, ↑ bruxism, shorter weekend sleep time	No information on BMI @ time of inj	Description: .5 Follow-up: 0
Reference	**Study Objective**	**Research Design**	**Sample Size Inclusion/ Exclusion**	**Subjects**	**Data Collection Methods/ Measures**	**Significant Findings**	**Comments**	**Quality**
Neuropsychology								
Mahmood et al., 2004 US	Type Neuropsychology Examine the relationship between sleep disturbances and neurocognitive ability post TBI	**Level IVA** Recruitment: Consecutive AI (archival records) Correlational Cross sectional	TBI = 87 Inclusion: • TBI diag based on medical exam, recovery to post-acute phase, medically determined need for rehab, cognitive function at Level VI (Levels of Cognitive Function Scale) • indication of at least a concussion (LOC or confusion or positive neuroimaging) Exclusion: NI	**Age:** NI **Gender:** 43.7% F **GCS:** mild: 24; mod 19; sev 44 **Time since:** 97% within a year of injury; 89.7% within 6 mo; 70.1% within 3 mo	PSQI BDI Global scale from Memory Assessment Scales Neuropsychology tests: Wide-range Achievement test (WRAT-3) – estimate of pre morbid IQ Digit Span Digit Symbol Grooved Peg Board Block Design Trail making-B Controlled Oral Word Association Test (COWAT)	37% had sleep disturbances mTBI more sleep disturbed than severe Performance on selected measures of cognitive function ↑ prediction of sleep disturbance accounting for 14% of variance beyond that accounted for by inj severity and gender (17%) executive functioning and speed of information processing difficulties may be associated with sleep disturbances	PSQI better at identifying insomnia but may have not have captured hypersomnia Need a reliable indicator better able to detect and report sleep disturbances Need to further assess the influence of gender; explore the threshold level and changes over time	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size:1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Wilde et al., 2007 US	Type Neuropsychology Examine the impact of	**Level III** Recruitment: PA (3 centres, sleep disorder	TBI = 35: OSA = 19 No OSA=16	**Age:** > 18 yrs **Gender:** OSA: 11%F No OSA: 25%F	Neuropsychological performance: Psychomotor Vigilance test Rey Complex	OSA ↓ on verbal and visual delayed-recall measures and > attention lapses	Strengths: First study to address this issue	**Moderate:** 4/7 Baseline: 1

	comorbid OSA on cognitive function of persons with TBI	centres and a rehab prog) Case controlled Cross sectional 2 TBI grps: OSA and No OSA Controlled using age, education, time post inj, and severity of inj and GCS (when avail) OSA diagnosed by nocturnal PSG	Inclusion: • > 18 yrs • ≥ 3 mos post-inj Exclusion: NI	**GCS:** OSA 53% unknown, 16% mod, 5% mod-sev, 26% sev No OSA: 50% unknown, 12% mod, 19% mod-sev, 19% sev **Time since:** ≥ 3 mos post-inj	Figure Rey Auditory-Verbal Learning Digit Span from WMS-R Finger tapping ESS on night of PSG and MSLT	Effect sizes using Cohen d: were medium and large	OSA associated with more impairment of sustained attention and memory Treatment of OSA did not improve outcomes Limitations: Lacked data on levels of severity, difficult to generalize findings Small N but effect sizes good	Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Wiseman-Hakes et al., 2010 Canada	Type: Neuropsychology Assess aspects of cognition and communication over a course of treatment for post traumatic hypersomnia (PTH)	**Level IVA** Recruitment: LC Single case study Treatment: 17 wks 1. Baseline: 12 mo post inj - Lorazepam 1 mg and Citalopram 20mg for 1 mo 2. At 1 yr1mo : Citalopram ↑40mg 3. At 1 yr2mo: add Ritalin 20mgs 4. At ↑40mg daily 5. Sleep Study 2: modafinil replace Ritalin and mirtazepine was	TBI= 1	**Age:** late teens **Gender:** male **GCS:** initial 3, hospital 5 PTA > 1 mo **Time since:** 11 mos	Daily Cognitive-communication and Sleep Profile (D-CCASP) ESS Stanford Sleepiness Scale PSG Maintenance of Wakefulness Testing (MWT) (at follow up)	Relationship between quality of sleep and language processing Prolonged REM latency Positive relationship between sleep and language processing, sustained attention/vigilance, memory and changes in medication Able to improve daily functioning and resume attendance at school	Limits: Single case study and exploratory in nature	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 0.5 Description: 1 Follow-up: 1

		added Baseline, 17 wks daily data collection, follow up at 3 yrs 8 mos						
Henry et al., 2000 US	Type Neuropsychology To Investigate neuropsychological, psychological and behavioural functioning following non-impact BI	**Level V** Recruitment: Retrospective OR Cross sectional Interviewed at one point in time Compared with published norms	Non-impact TBI=32 Inclusion: • History of whiplash with brief or no LOC and no evid of cranial trauma • No physical evid that head struck windshield/headrest • Subj report of an alteration in mental status at accident with no obj evid Exclusion: Previous whiplash or closed BI, neurological disorder, seizure, psychiatric problem, substance abuse or medical condition or medication that compromise nervous system integrity	**Age:** 18-64; mean 41.8 yrs **Gender:** 53% F **GCS:** NI **Time since:** 1 wk to 5 yrs	Clinical interviews corroborated via interviews with significant others/ coworkers Neuropsychology battery: Wechsler Adult Intelligence Scale – revised (WAIS-R), WMS-R, Rey figures, Hooper, Boston naming and verbal fluency, Trials A and B, Wisconsin Card Sort, Strop, auditory consonant trigrams, PASAT	Cognitive deficits observed particularly with executive functioning (attention and concentration) PASAT most sensitive test Some experience of mild depression Problems observed with behavioural control, sleep and sexuality EEQ showed front-central slowing and ↑ in spike activity	Whiplash can produce wide-ranging circuitry dysfunction (similar to mTBI)	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: .5 Follow-up: 0

Reference	Study Objective	Research Design	Sample Size Inclusion/ Exclusion	Subjects	Data Collection Methods/ Measures	Significant Findings	Comments	Quality
Intervention								
Jha et al., 2008 US	Type Intervention Test the efficacy of modafinil in treating fatigue and EDS	**Level II** **Downs and Black:** 23/28 Recruitment: PA double blind, placebo-controlled crossover trial: 4 wk washout period, 4 wk open label trial at end modafinil: 2 x 100 mg twice a day for 8 wks with 2 wk graduated in (manufacturer provided) data collection: baseline, week 4, week 10, weeks 4 and 10 after crossover	E1 = 24 (drug first) E2 = 22 (placebo first) Inclusion: • 1 yr post-TBI (severe enough to require inpt rehab) • 18-65 yrs • Report fatigue and/or EDS compromising functioning Exclusion: • neurologic/neuron psychiatric diag • Other diag for EDS • Concurrent sig systemic disease • Epilepsy • Cardiovascular disease • Sig psychiatric or behaviour symptoms • Non-English • Pregnant females or potential child-bearing unless using contraceptives	Age 38.25(12.20) **Gender:** 31.4% F **GCS:** severe: 3-8 (51%); moderate 9-12 (23.5%); mild 13-25 (25.5%); **Time since:** 5.77±4.97 yrs	Modified Fatigue Impact Scale Fatigue Severity Scale ESS MOS-12 item SF-12 Post Concussion Assessment Cognitive Testing (Impact) Connor's continuous performance test II BDI II	ESS: E1>E2 at week 4 but not at week 10: only short term beneficial Insomnia reported more often with drug than placebo Safe and well-tolerated There was no sig differences between modafinil and placebo and no consistent and persistent clinically sig differences	Strengths: Thorough complete information with demographics, methodology Acknowledged complexity of fatigue and relationship with sleepiness Limitations: All sleep measures self-report Standard dosage therefore not able to tailor to individual (modify to meet individual responses (ex. taper) Single center Multiple stat tests, Clinical sig complicated as most did open label	**High:** 6.5/7 Baseline: 1 Blinding: 1 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 1
Castriotta, 2008 USA	Type Intervention Determine	**Level III** **Downs and Black:** 17/28	TBI = 57 Inclusion: • > 18 yrs	**Age:** 38.6 ±14.8 yrs **Gender:** 25% F	Sleep : NPSG MSLT ESS	39% had abnormal sleep studies :23% OSA, 3% PTH,	Strengths: Rigorous methods; used established	**Moderate**: 5/7 Baseline: 1

	whether treatment of sleep disorders identified in BI adults results in resolution of those disorders and improvement of symptoms and daytime function	Recruitment: Prospective unselected pts AI (3 centres) Longitudinal Baseline and 3 mos; neuropsychological testing performed at 10:30 to control for diurnal variation; only those with sleep disorder did the sleep assessment again at 3 mos	• ≥ 3 mo post inj Exclusion: • Presence of circadian rhythm disorder • Unable to give informed consent • Use of sedating medications	**GCS:** used with CT findings according to criteria to establish severity 30% sTBI; 5% mod-sTBI; 18% mod TBI; 9% mTBI; 38% missing **Time since:** 67.8 ±126.3 mo	Neuropsychological : PVT POMS FOSQ Urine sample to test for drugs/medications Treatment : CPAP for OSA Modafinil for narcolepsy and PTH Pramipexole for Periodic Limb Movement Syndrome (PLMS)	5% narcolepsy, 7% PLMS 21% EDS GCS ↓ for sleep disordered Sleep disordered > reductions in tension and anger and ESS than non-disordered Apnea/hypopnea Index improved with treatment ↑ Amount of REM Treatment may result in NPG resolution without change in sleepiness of neuropsychological function	criteria as much as possible Limitations: Medications not titrated Large missing severity data Subsamples small MSLT not the right measure as it seems that sleep and wakefulness are 2 separate active processes	Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 1
Francisco & Ivanhoe, 1996 US	Type: Intervention Effects of methylphenidate on post traumatic narcolepsy	**Level IVA Downs and Black:** 11/28 Recruitment: LC Single Case Study Methylphenidate: 10mg 2x/day then ↑ to 30mg 2x/day over 4 mos	TBI=1 Classic tetrad of narcolepsy (cataplexy, EDS, sleep paralysis, hypnogogic hallucinations); diag confirmed by PSG and MSLT No structural, metabolic, or cardiac abnormalities that explain the symptoms	**Age:** 27 yrs **Gender:** Male **GCS:** 3 at inj site but 7 at ED; mod TBI **Time since:** 22 mo	PSG MSLT	1 mo after initiation cataplexy and EDS started to improve 6 mo after the start of treatment the pt is asymptomatic At 12 mo medications was involuntarily withdrawn and symptoms returned	Drugs leading to norepinephrine release may be helpful in reversing the symptoms of narcolepsy	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 1

Ouellet & Morin, 2007 Canada	Type Intervention Determine the efficacy of cognitive behaviour therapy (CBT) in TBI	**Level III** **Downs and Black:** 16/28 Recruitment: OR Single case design with multiple baselines across subjects 8-wk CBT addressing stimulus control, sleep restriction, cog restructuring, sleep hygiene, education and fatigue management Sleep diary for 2 wks at follow up and baseline, 3 , 5 or 7 wks randomly determined across subgrps of 3 1 and 3 mo follow up	TBI = 11 Inclusion: • 18-50 yrs • TBI in last 5 yrs • Not an inpt • Insomnia syndrome (operational definition) • If on meds for 6 mos and stable Exclusion: • Major untreated or unstable medical or psychiatric co-morbidity • Meds known to prod insomnia • Sleep disturbances before TBI • Another sleep disorder • Unable to complete questionnaire • Experience sig pain	**Age:** 27.3 yrs **Gender:** 46% F **GCS:** 3-14; 2 no data; m to sTBI as evaluated by multidisciplinary team using standard criteria **Time since:** 25.64 mos	Sleep diary (Total wake time, Sleep efficiency) Diagnostic Interview for Insomnia ISI MFI Dysfunctional Beliefs and Attitudes about Sleep Scale BDI BAI 2 night PSG Short telephone interview at follow-up by independent interviewer	Baseline results showed variability as expected Clinical and sig reductions in total wake time and sleep efficiency for 8/11 (74%) Prog generally well maintained at follow-up Sleep efficiency augmented ↓ fatigue symptoms	Strengths: Good baseline table CBT seems promising Limitations: Needed to include description of CBT Did not assess cognitive functioning Women were over-represented Self-selected so may be more motivated to change.	**Moderate**: 4.5/7 Baseline: 0.5 Blinding: 0.5 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: .5 Follow-up: 1
Ouellet & Morin, 2004 Canada	Type Intervention To test the efficacy of CBT for insomnia with TBI in a person with difficultly falling asleep and staying asleep since inj	**Level III** **Downs and Black:** 10/28 Recruitment: OR Single case study 8 wkly individual manualized CBT	N = 1 Diagnostic clinical interview determined that had mixed insomnia (ICSD and DSM)	**Age:** late 30s **Gender:** male **GCS:** 13/15, no coma, PTA 5-7 days, moderate TBI **Time since:** NI	Sleep diary for 5 wks of baseline 8 wks CBT, 2 wk post treatment and follow up at 1 and 3 mos PSG (5 nights: 3 pre and 2 post) Insomnia Severity Index (ISI) Dysfunctional Beliefs and	Sleep onset ↓ from 47 minutes to 18 and nocturnal awakenings ↓ from 85 to 28 minutes; both below clinical criteria Sleep efficiency ↑ from 58% to 83%	Strengths: Was adapted for TBI The behavioural recommendations in the intervention were simple and straight forward Promise for non-	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1

		sessions (adapted for TBI) addressing stimulus control, sleep restriction, cog restructuring and sleep hygiene education given by a clinical psychologist 5 wks of baseline, 8 wks CBT, 2 wk post treatment and follow up at 1 and 3 mos			Attitudes about Sleep Scale MFI BAI	PSG corroborated data Majority of gains were maintained at follow up (tapering of med was occurring) ISI dropped from clinical to sub-clinical score	pharmacological interventions, particularly CBT	Standardized outcomes: 0.5 Description: 1 Follow-up: 1
Shan & Ashworth, 2004 Canada	Type Intervention Assess the effects of lorazepam versus zopiclone on cognition	**Level II** **Downs and Black:** 23/28 Recruitment: Consecutive AI Double blind, crossover trial Self regulate (0, ½, or full tablet) of lorazepam (.5-1.0 mg) or zopiclone (3.75-7.5 mg) at bedtime for 7 days Starting dose randomly generated At 2 wks state which intervention prefer	ABI and stroke = 18 (ABI: 6) E1=9 E2=9 Inclusion: • > 18 yrs • Secondary causes of insomnia OK: depression, apnea, restless legs Exclusion: • acutely ill • Non-English/French • Unable to read questions • Severe cognitive impairment	**Age:** 56.6 yrs **Gender:** 44% F **GCS:** NI **Time since:** NI	Folstein MMSE: baseline, during week 1 and week 2 Rate quality of sleep from night before (2 of 7 days but not the first 3 days) – locally developed Total sleep time recorded by nursing staff q 30 mins or 1 hr Nurses rated restfulness and drowsiness on a 1-4 scale Testing for ataxia	The medications seem to be equally effective	Limitations: Non-pharmacological interventions used Criteria participants used for self dosing not clear Weak measures: locally developed as convenience, thought more sensitive than Morning Sleep Questionnaire and no gold standard Excluded severe impairment	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 1 Sample size: 0 Attrition: 1 Standardized outcomes: 0 Description: 1 Follow-up: 0

Reference	Study Objective	Research Design	Sample Size Inclusion/ Exclusion	Subjects	Data Collection Methods/ Measures	Significant Findings	Comments	Quality [a]
Epidemiology / Prevalence/Description: Comparison Group								
Fichtenberg et al., 2002 US	Type Epi/Prev/Desc Establish frequency of insomnia (diagnosis using DSM-IV) in TBI and compare it to insomnia rates in other rehab outpts	Level **III** Recruitment: Prospective cohort Consecutive OR Cross-sectional Comparison group (C): rehabilitation outpatients (same # spinal cord injury (SCI) and musculoskeletal (MSK))	TBI [b] =50 C=50: MSK=25; SCI=25 Inclusion: • Galveston Orientation and Amnesia Test (GOAT) > 75 • ≥ Rancho Los Amigos Level VI Exclusion: • not in PTA state	**Age:** (p<0.05) TBI 36.5±14.5 yrs; SCI 38.2±13.5; MSK 47.3±12.2 **Gender:** (p<0.05) TBI 44%F; SCI 24%F; MSK 80%F **GCS:** sTBI 42%; modTBI 18%; mTBI 40% **Time since:** 3.8±7.4 mos	PSQI BDI Sleep diaries (TBI only) Insomnia diag using DSM-IV criteria	TBI: ↓ sleep quality (initiation probs 2x duration probs); ↑ sleep duration TBI: 30 % insomnia diag (DSM-IV) TBI: ↓ PSQI global scores TBI: < insomnia rate than C	Prevalence of insomnia is 1/3 of TBI population First paper to use formal diagnosis of insomnia Limitations: Did not stratify results by severity Reliability of self-report sleep diaries	**Moderate:** 4.5/7 Baseline: 1 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Parcell et al., 2006 Australia	Type Epi/Prev/Desc Explore subj sleep reports from persons with TBI	Level **III** Recruitment: Consecutive PR (≥ 2 wks post d/c) Longitudinal Survey design C: general community, age and gender matched TBI reflect on changes since	TBI=63 C=63 Inclusion: • 16-65 yrs • facility in English • No transmeridian travel across > 1 time zone in previous 12 mos • No pre-inj sleep disorder • No benzodiazepines or other sleeping medications • No previous BI, neurological disorder or major	**Age:** TBI 32.5±1.7 yrs; C 30.5±1.2 **Gender:** both grps 43% F **GCS:** 9.6±.57 PTA 19.8± 2.7: used for severity mTBI = 8; modTBI = 13; sTBI = 27; vsTBI = 14 **Time since:** mean 230 days	7-day self report sleep-wake diary (sleep and wake times, sleep onset latency, frequency, and duration of nocturnal awakenings and daytime naps) general sleep questionnaire to evaluate sleep changes and quality ESS HADS	TBI: > sleep changes; > night-time awakenings and longer sleep onset latency; more frequently reported by mTBI ↑ anx and dep assoc with↑ reporting of sleep changes	Strengths: Follow up and used a 7-day diary Considered other potential factors impacting sleep Limitations: Difference in time used to note changes (TBI 8 mos; C 3 mos)	**Moderate**: 4.5/7 Baseline: 1 Blinding: 0 Sample size: .5 Attrition: 0 Standardized outcomes:1 Description: 1 Follow-up: 1

		inj and C reflect on changes in the last 3 mos Data collection: initial and 3 mos	psychiatric disorder Screened by neuropsychologist to determine eligibility					
Watson et al., 2007 US	Type Epi/Prev/Desc Evaluate the prevalence of sleepiness following TBI	Level **III** Recruitment: Prospective cohort Consecutive A Longitudinal 2 Comparison grps; C1 non-cranial trauma admissions; C2 trauma free selected from friends of TBI Data collection: 1 mo and 1 yr post inj	TBI = 512 (N=346 @ 1 mo; N=410 @ 1yr) C1= 132 (N=131 @ 1 mo; N=124 @ 1yr) C2= 102 (N=101 @ 1 mo; N=88 @ 1yr) Inclusion: • Any period of LOC • PTA≥1hr • Other obj evidence of head trauma • Hospitalization ** some had pre-existing conditions: prior TBI, alcohol abuse, sig psychiatric disorder	**Age:** TBI 30±14yrs; C1 31.4±13.5; C2 24.5±8.1 **Gender:** TBI 27%F; C1 28%F; C2 56% F **GCS:** ≤ 10 at admission Inj severity: time from inj to a consistent GCS score of 6 **Time since:** 1 mos & 1 year at follow-up	Sickness Impact Profile (SIP): sleep and rest subscale consisting of 4 questions	TBI: 55% endorsed ≥1 sleepiness items 1 mo post inj vs C1 41% and C2 3% TBI: 27% endorsed ≥1 sleepiness items 1 yr post inj vs C1 23% and C2 1% TBI: sleepier than C1 at 1 mo but not 1 yr TBI are sleepier particularly those with more severe injuries; sleepiness ↓ in TBI but about 25% remain sleepy after 1 yr (also true for C1)	Strengths: Good follow up Limitations: Weak outcome measure; not separately validated; just descriptive data, large attrition Majority were mTBI as sTBI not able to complete the SIP; may lead to underestimate of the true sleepiness pattern in TBI	**Moderate**: 4.5/7 Baseline: 1 Blinding: 0 Sample Size: 1 Attrition: 0 Standardized outcomes: .5 Description: 1 Follow-up: 1
Beetar et al., 1996 US	Type: Epi/Prev/Desc Compare the incidence of sleep and pain in TBI and comparative neurologic populations	Level **III** Recruitment: OR (neuropsychology service) Cross sectional Case control study Consecutive chart review	mTBI= 127 mod to sTBI = 75 C=123 Used Mild TBI Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine	**Age:** TBI 36.1±11.7; C 43.3±13.6 **Gender:** TBI 32%F; C 42% F **GCS:** NI **Time since:** TBI 23.9±2.2 mos (inj); C 35.5±23.3 mos (symptom)	Chart review Patient report of sleep and or pain problems	Sleep maintenance most common sleep problem TBI: 55% had insomnia complaints vs C < 33% TBI: > insomnia and pain complaints (2.5 x more); presence	Strengths: One of earliest studies to document incidence Limitations: Retrospective and subj data collection	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 0

		Comparison group: general neurologic pts referred for neuropsychological assessment				of pain ↑ insomnia report 2x TBI without pain: > sleep complaints than C and mTBI >mod/sTBI mTBI > pain than mod/sTBI Complaints ↓ with > time since inj		Description: 1 Follow-up: 0
Ouellet & Morin. 2006 Canada	Type: Epi/Prev/Desc: Compare subj and obj measures of sleep in TBI	Level **III** Recruitment: LC (rehabilitation centres and advertisements sent to TBI associations and support grps mailing lists) Cross sectional Comparison Group: healthy good sleepers matched on age and gender to TBI; recruited through advertisements and acquaintances of the authors 2 nights of PSG	TBI = 14 m to sTBI C = 14 Inclusion: • 18-50yrs • TBI ≤ last 5 yrs • Stable phys health • No longer an inpt • Have an insomnia syndrome Exclusion: • Major untreated or unstable co-morbid condition • Sleep difficulties before TBI • Evidence of another sleep disorder • Sig pain • Unable to complete the questionnaires	**Age:** TBI 30.4±9.7 yrs; C 30.0±10.0 **Gender:** 56% F **GCS:** 4 mild, 1 mild-mod, 4 mod, 3 mod-sev, 2 sev (criteria in article) **Time since:** 21 mos	Diagnostic Interview for Insomnia Sleep dairy PSG Sleep survey ISS MFI BDI Beck Anxiety Inventory	TBI: PSG showed 71% with insomnia Large effect sizes for total sleep time, wake after sleep onset, awakenings longer than 5 min, and sleep efficiency TBI: > proportion of stage 1 sleep When those using psychotropic meds excluded, TBI had > awakenings lasting longer than 5 min and a short REM sleep onset latency	Results similar to those with primary insomnia or insomnia related to depression Limitations: Small sample size and a lot of variability in TBI grp and presence of sleep problems in control grp Multiple comparison and lack of statistical power	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Parcell et al., 2008 Australia	Type Epi/Prev/Desc Evaluate changes in sleep quality and changes in	Level **III** Recruitment: AI (mod to sTBI) Cross sectional	TBI =10 C=10 Inclusion: • 16-65 yrs • English facility	**Age:** TBI 38.8±4.3; C 37.8 ±44.4 **Gender:** 40% F **GCS:**	Demographic and medication details at recruitment and inj details from medical records	TBI: poorer sleep quality and higher levels of anx and dep TBI: ↑ in deep	Documents importance of subj report as central to diag and treatment but need to	**Moderate:** 4/7 Baseline: 1 Blinding: 0

	obj recorded sleep parameters after TBI and investigate the relationship between mood state and injury characteristics	Survey and lab-based nocturnal PSG Comparison group: age- and gender-matched controls in general community PSG over 2 nights within 1 wk; evaluated in TBI and C pairs	• Normal body mass index • No trans-meridian travel across > 1 time zone in previous 12 mo • No pre-inj sleep disorder • No benzodiazepines or other sleeping medications • No previous BI, neurological disorder or major psychiatric disorder •	10.9±1.0 40% mod TBI; 40% sTBI; 20% vsTBI PTA 16.44±4.3 days **Time since:** 516±124 days	Sleep-wake diary for 7 days ESS Sleep quality questionnaire (TBI changes since inj and C changes in last 3 mos) PSQI Nocturnal PSG HADS	(slow wave) sleep, ↓ in REM, > night-time awakenings TBI: > anx and dep which co-varied with the observed sleep changes	consider obj data as well Provides many important practice points; is a strong contributor to clinical and research literature	Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Schreiber et al., 2008 Israel	Type Epi/Prev/Desc: Identify the characteristics of sleep disturbance in adults after mTBI	Level **III** Recruitment: Retrospective Consecutive OR (where sleep lab data available) Cross sectional Comparison Group: matched and referred for sleep evaluation as part of routine pre-employment assessment TBI 2 nights PSG (not on a weekend); C only 1 night MSLT on day between the 2 nights	mTBI = 26 C=20 (apparently healthy) Inclusion: • 21-50 yrs • Documented (≥ 1 yr since mTBI • Normal brain CT, MRI • Negative electroencephalogram (EEG) • No past history of CNS pathology • No pre-morbid or present major psychiatric diag • No sleep apnea or restless legs syndrome	**Age:** TBI 31.6±8.8 yrs; C 33.8±7.8 **Gender:** NI **GCS:** NI **Time since:** 12 mos to 21 yrs	PSG MSLT	TBI: sleep patterns disturbed; sleep architecture altered: < REM sleep scores and > NREM scores TBI: MSLT documented sig EDS	Important to identity those who need treatment for sleep problems Limitations: C were not all within the normal values Possible issues of recall bias Wide range of time post inj Difference in data collection strategy between the two grps	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Williams et al., 2008	Type: Epi/Prev/Desc	Level **III** Recruitment:	TBI = 9 C = 9	**Age:** TBI 21.4±2.4; C 20.7±2.1	Personality Assessment Inventory (PAI):	TBI: long-term trouble with initiating/	Sleep disturbances can persist well after	**Moderate:** 4/7

Canada	Characterize the extent and nature of disrupted sleep in individuals with long-term sleep complaints subsequent to mTBI (i.e., sport-related concussion) To determine whether sleep disturbances in mTBI are more characteristic of psychological, psychiatric, or idiopathic insomnia	LC (university setting) Cross sectional Comparison Group Face-to-face interview and laboratory PSG	Inclusion: • 18-26 yrs TBI: • Between 6 mos and 6 yrs post-inj • symptoms of Post Concussion Syndrome (PCS) at the time of inj • clearly distinguish between sleep patterns before and after inj • sleep difficulties within 1 mo of inj • sleep complaints characterized by sleep onset of > 30 mins on ≥ 4 or days in a wk C: • no previous BI • No sleep difficulties	**Gender:** TBI 33%F; C 56% F **GCS:** mild range; LOC for ≤ 5 minutes **Time since:** TBI 27.8 ±15.5 mos	dep and anx Brock Adaptive Functioning Questionnaire (BAFQ) PSQI Sleep Disorders Questionnaire (SDQ) Brock sleep and insomnia questionnaire Sleep log for 2 wks PSG for 3 consecutive nights Power spectral (FFT) analysis of the sleep onset period	maintaining sleep with attention and memory and affective (dep and anx) abnormalities; sig diff shown in PAI, BAFQ, PSQI TBI: 4% less efficient sleep, shorter REM onset latencies, longer sleep onset latencies (variability within sample); FFT revealed greater intra-subject variability in sigma, theta and delta power during sleep onset TBI different from C but not easily classified into existing insomnia subtypes	injury Strengths: Very thorough study Limitations: Small N, sample of convenience (student volunteers) Confirmation of subj self-reports with PSG Highlights need to look at sport-related concussion	Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Gosselin et al., 2009 Canada	Type: Epi/Prev/Desc Investigate the effects of sport-related concussion on subj and obj sleep quality	Level **III** Recruitment: LC (independent of the nature of reported symptoms) Cross sectional Used concussion diagnostic criteria Comparison group: No history of concussion; matched on age,	ABI = 10 C = 11 Inclusion: • ABI: history of at least 2 concussions Exclusion: • Presence of neurological or psychiatric diseases • Extremely early or late habitual bed times • Use of drugs known to affect sleep or daytime	**Age:** ABI 24.3 ± 6.1 yrs; C 22.6 ± 2.4 **Gender:** ABI 30%F; C 34% F **GCS:** ABI all 13-15 # concussions: 4.6±2.1 with at least 1 in last yr **Time since:** NI	PSG QEEQ: assessment of 10-min period of wakefulness 30-mins after sleep offset Post Concussion Symptom Scale (PCSS) PSQI ESS BDI Local developed questionnaire on sleep quality Cog Sport computer battery:	ABI: >symptoms, worse sleep quality; > delta activity and < alpha activity during wakefulness Concussion seems to be associated with a wakefulness problem rather than sleep disturbance Athletes with worse sleep quality (PSQI) and	Discrepancy between subj and obj findings; not explained by depression nor hyper arousal Limitations: Small sample and with exclusions the sample became even smaller however, highlights need to assess sleep and wakefulness following sport-related	**Moderate:** 4/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

		gender, education and age started playing the sport PSG on 2 consecutive nights in the lab	sleepiness • Work the night shift • Travel to another time zone in last 2 mos		short neuropsychology evaluation adapted from National Football League battery	symptoms (PCSS) > relative delta power during daytime; ABI lower PSQI associated with ↓ in REM sleep efficiency PSQI and PCSS correlated Absolute spectral power showed high inter-subject variation in ABI therefore analyze on the relative spectral power	concussion Only a pilot study	
Reference	**Study Objective**	**Research Design**	**Sample Size** **Inclusion/ Exclusion**	**Subjects**	**Data Collection Methods/ Measures**	**Significant Findings**	**Comments**	**Quality**
Epidemiology / Prevalence / Description: Cohort/Single Group								
Baumann et al., 2007 Switzerland	Type: Epi/Prev/Desc Determine the frequency and clinical characteristics of post-traumatic sleep-wake disorder (SWD); assess cerebral spinal fluid (CSF) hypocretin levels 6 mos after TBI and risk factors for post traumatic SWD.	**Level III** Recruitment: Prospective study Consecutive A (within 4 days of inj) Longitudinal Single Group Baseline: laboratory tests 6 mo: other outcomes, subsample repeated laboratory tests	TBI= 65 (96 enrolled; 76 available for follow-up) Inclusion: • acute, first ever TBI Exclusion: • sleep-wake or psychiatric disorders diagnosed prior to TBI	**Age:** 16-72, mean 38± 16 yrs **Gender:** 14% F **GCS:** mean 10.2, mTBI: 40%; modTBI: 23%; sTBI: 37% **Time since:** 6 mos after TBI	CT scan CSF hypocretin-1 levels Human leukocyte antigen (HLA) typing Interview: social status and residual symptoms post inj, including sleep habits Neurological examination using a standard protocol, with the Folstein Mini Mental Status Examination (MMSE) BDI	SWD are common after TBI, EDS/fatigue = 55% Post traumatic hypersomnia = 22% Low hypocretin levels found in 19% 6 mos after inj vs 93% in first days after inj 6 mo hypocretin levels were lower in those with post traumatic SWD No other sig relationships were found	Strengths: Very thorough Limitations: Attrition was large and not all available for laboratory follow up	**High:** 5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 0.5 Standardized outcomes: 1 Description: 1 Follow-up: 1

					Medical Outcomes Study Short Form – 36 ESS Sleep Apnea Scale of the Sleep Disorders Questionnaire Ullanlinna Narcolepsy Scale Swiss Narcolepsy Scale PSG MSLT Actigraphy.	Hypocretin system possible contributor to pathophysiology of post traumatic SWD		
Castriotta et al.,2007 USA	Type Epi/Prev/Desc Determine the prevalence and consequences of sleepiness and sleep disorders after TBI Explore relationship between presence of sleep disorders, inj characteristics and subject variables	**Level IV A** Recruitment: Prospective study AI (3 centres) Single Group Cross sectional	TBI=87 Inclusion: • > 18 yrs old • ≥ 3 mos post inj Exclusion: • presence of circadian rhythm disorder • use of sedating medications • unable to give informed consent	**Age:** 38.3± 15.1 **Gender:** 28% F **GCS:** NI Severity: Mild 8%, moderate 175, moderate-severe 6%, severe 33%, unknown 36% **Time since:** 64.3±117.7 mos	PSG MSLT ESS Psychomotor Vigilance Test (PVT) Profile of Mood States (POMS) Functional Outcome of Sleep Questionnaire (FOSQ)	23% OSA 46% Abnormal sleep studies 11% post traumatic hypersomnia 6% narcolepsy 7% periodic limb movements 25% with obj EDS No correlation between ESS and MSLT(r=0.10) No differences in demographics and inj chars between sleepy (Sl) and non-sleepy (NSl) Ss BMI: Sl >NSl PVT: Sl<NSl FOSQ: Sl better NSl POMS: no differences	Strengths: First study to show that a sleep disorder adds an additional cognitive burden Limitations: No obj measure of daily functioning	**High:** 5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

Fichtenberg et al., 2000 USA	Type: Epi/Prev/Desc Relationship between insomnia and demographics, injury and psychological variables in post-acute TBI	Level IV A Recruitment: Prospective study Consecutive OR Cross sectional Single Group	TBI=91 Inclusion: • diag of TBI on basis of examination • recovery to post-acute phase • medical determination of need for outpt neurorehabilitation Exclusion: • in state of PTA • rated below Level VI on Levels of Cognitive Functioning Scale (LCFS) • using sleep medication •	**Age:** 33.8± 14.5 yrs **Gender:** 41% F **GCS**: 13-15: 33% 9-12: 21% 3-8: 46% **Time since**: mean 3.3 mos	PSQI BDI GOAT LCFS	Strong relationship between insomnia and depression. Pain disturbance of sleep was sig associated with insomnia. BDI : 68% depressed were suffering with insomnia	Strengths: Identifies a developmental pattern that may progress from a physiological basis to a secondary disorder associated with depression	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Ouellet, Beaulieu-Bonneau, & Morin, 2006 Canada	Type: Epi/Prev/Desc To determine the frequency of insomnia according to DSM-IV and International Classification of Sleep Disorders (ICSD) criteria. To describe clinical and socio-demographic characteristics of insomnia in TBI	**Level IVA** Recruitment: LC (French-speaking from rehabilitation centre archives and on mailing lists of TBI associations in Quebec) Mailed questionnaire Cross sectional Single Group Significant others completed a brief parallel evaluation	TBI=452 Inclusion: • ≥16 yrs • TBI: minor, mild, moderate or severe	**Age:** 40.2 ±13.1 yrs **Gender:** 35% F **GCS:** NI Severity: 59.9% sTBI 23.3% modTBI 13.7% mTBI (criteria includes GCS) **Time since:** mean 7.8 yrs	Questionnaire booklet entitled "Quality of sleep and level of fatigue following a TBI": Locally developed questions ISS Multi dimensional fatigue inventory Indice de détresse psychologique de L'Enquête Santé Québec (French adaptation of Psychiatric Symptom Index) Significant Other's Evaluation Questionnaire (significant other versions of ISS and other above	Insomnia prevalent after TBI, 64.3% with sleep onset insomnia, 76.6% with sleep maintenance insomnia Predictors of insomnia: lesser severity of BI, depressive symptoms, self-reported pain, fatigue	Limitations: Only subj data Under-representation of mTBI Those with insomnia problems may have been more motivated to respond Not able to determine insomnia subtypes	**Moderate:** 4.5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 0.5 Description: 1 Follow-up: 0

					questions)			
Rao et al., 2008 USA	Type: Epi/Prev/Desc To assess the prevalence of and risk factors for sleep disturbances in acute post-traumatic TBI	**Level III** Recruitment: PAC (within 3 mos of trauma) Longitudinal observational study Single Group Data collection: 1. within 2 wks of inj to assess history of psychiatric and sleep problems; 2. within 1-3 mos of inj; for some both at the same time	TBI=54 Inclusion: • ≥18yrs • able to provide informed consent • admitted to hospital with experience of LOC • GCS ≤ 15 • Positive CT findings Exclusion: • prior TBI • open head injury • history of other type of illness	**Age:** 43.2± 17.7 yrs **Gender:** 41% F **GCS:** mean 12.5± 3.6 65% mild, 11% moderate, 19% severe **Time since:** ≥ 3 mos	Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID-IV) General Medical Health Rating Scale (GMHR) MOS Self-report for anx and dep	Worse on most sleep measures after TBI compared to before TBI Anx disorder secondary to TBI was most consistent sig risk factor to be associated with worsening sleep status	Strengths: Assesses sleep problems in the acute period Participants had a range of severities Limitations: Subj data and recall bias might be an issue Lack of info on other potential influencing factors (pain, medical problems, and medications)	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0.5
Clinchot et al., 1998 USA	Type: Epi/Prev/Desc Define and correlate the incidence and type of sleep disturbances that occur after BI	**Level V** Recruitment: Prospective study Consecutive AI Single Group Longitudinal Baseline and 1 yr follow up post d/c via telephone interview	TBI=145 Inclusion: • ≥14 yrs with sustained BI Exclusion: • Not acute inj • Primarily the result of anoxia	**Age:** 31 yrs **Gender:** 23% F **GCS:** median=4 **Time since:** mean 20 days	Direct observation Medical Record extractions Agitated Behaviour Scale FIM Wechsler Memory Scale (WMS) Halstead Reitan Neuropsychological Battery Follow up interview: Community Integration Questionnaire Sleep difficulties, medical problems, medications, services used	50% diff with sleep, 25% sleeping more and 45% diff falling sleep GCS≤ 7 less likely to have problems with sleep than GCS>7 64% with sleep diff waking up too early Sleep complaints correlated with presence of fatigue, > GCS, better immediate memory, positive substance abuse history, > age,	Limitation: Large number lost to follow up; those lost more likely to have a history of substance abuse Self-report of sleep difficulties	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 0 Standardized outcomes: 1 Description: .5 Follow-up: 1

						and being female		
Webster et al., 2001 USA	Type Epi/Prev/Desc Determine the occurrence and nature of sleep related breathing disorders in adults with TBI	**Level IV A** Recruitment: Prospective observational study Consecutive AI Single Group	TBI=28 Inclusion: • 18-65 yrs • < 3 mos post inj • Rancho ≥ 3 Exclusion: • Previously documented sleep apnea, narcolepsy, or habitual snoring • Tracheostomy • History of other premorbid neurologic or pulmonary conditions	**Age:** 34.5 yrs **Gender:** 25% F **GCS:** lowest during the first 24 hrs; 71% GCS≤8 25% GCS 9-12 4% GCS >12 PTA >1 day Rancho 95% Level VI or VII **Time since**: < 3 mos	Overnight sleep study using portable 6-channel monitoring system; calculated a respiratory disturbance index (RDI)	Sleep related breathing disorders defined by a respiratory index of 5 or greater appears to be common in adult subjects with TBI. Evidence of sleep apnea was found in 36% of subjects.	Strengths: Prospective and consecutive design New info regarding the occurrence of sleep apnea in early recovery phase Attempt to eliminate confounding factors Limitations: Low power Homogeneous sample Not able to collect EEG data	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0.5 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Masel et al., 2001 USA	Type Epi/Prev/Desc Determine prevalence, demographics and causes of EDS in adults with BI and investigate relationship between subj and obj data	**Level III** Recruitment: Consecutive AI Case series Cross sectional Single Group 2 overnight sleep evaluations 1 wk apart; actigraphy for 2 wks after 2nd PSG	TBI=71 Complete medical history and physical examination Inclusion: None Exclusion: None	**Age:** 32±11 yrs **Gender:** 38% F **GCS:** only for 56%: Non hypersomnia (NH) 6±4; Post traumatic hypersomnia. (PTH) 7±5; Hypersomnia with abnormal indices (HAI) 8±5 Rancho ≥ Lev IV **Time since:** 38±60 mos	Actigraphy PSG MSLT ESS PSQI Millon Clinical Multiaxial Inventory - II (MCMI-II) Neuropsychologic battery Diag of narcolepsy and post traumatic hypersomnia using the ICSD	Hypersomnia was common with high presence of sleep apnea hypopnea syndrome, periodic limb movements and PTH NH: N=38; PTH: N=21; HAI: N=12 No relationship between hypersomnia grps and GCS, psychopathology, time post inj, and demographic variables; no sig differences of note on the neurologic tests	Suggest maybe that TBI have an inability to perceive their hypersomnolence Limitation: Wide range of time post inj Self-selection bias	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

						No sig correlation between ESS or PSQI and MSLT		
Verma et al., 2007 USA	Type Epi/Prev/Desc Determine the spectrum of sleep disorders in pts with chronic TBI and determine if the severity of sleep disorder is related to severity of chronic TBI.	**Level V** Recruitment: Retrospective LC (Referred for evaluation for sleep disorder) Cross sectional Single Group One overnight PSG	TBI=60 Inclusion: NI Exclusion: NI	**Age:** 20-69 yrs, mean 41 yrs. **Gender:** 37% F **GCS:** NI Severity assessed by GAF: mild 40% moderate 20% severe 40% **Time since:** 3mos-2 yrs	Detailed medical history, neurological exam, neck size, chin size and position, jaw alignment, and oropharyngeal examination PSG MSLT ESS BDI Hamilton Anxiety Scale	A full spectrum of sleep disorders occur in patients with chronic TBI Complicated relationship with severity of inj EDS was most common presenting symptom; which may lead to other problems like insomnia, anx and dep	Strengths: Identifies and describes the spectrum of sleep disorders Sleep disturbances can compromise rehab process and return to work Limitations: Retrospective 1 night of PSG Lack of exclusion of possible effects of meds and pain HAS and BDI not collected on all participants GAF may not be best evaluation of severity	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Castriotta & Lai, 2001 USA	Type Epi/Prev/Desc Determine the frequency of sleep disorders associated with TBI; investigate relationship between post traumatic sleep	**Level III** Recruitment: Prospective cohort study Consecutive yet timing post inj unclear Cross sectional	TBI=10 Inclusion: • subj excessive sleep • ≥ 18 yrs or older • alert and oriented Exclusion: • medications to cause	**Age:** 56.3± 5.3 yrs **Gender:** 60% F **GCS:** sTBI 60%, mTBI 40% **Time since:** ≥72 hrs; 110±191 mos	Clinical interview ESS PSG MSLT	Sleep disordered breathing was found in 7 subjects Overt OSA in 5 subjects Narcolpesy in 2 subjects	Strengths: Prospective Limitations: Small sample	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1

	disorders and pre-traumatic sleep disorders.	Single Group Use criterion standard to diag sleep disorders Those with overt sleep apnea had a 2nd PSG with titration of nasal continuous positive airway pressure	hypersomnolence • pregnancy • pts with cardiopulmonary and recent abdominal and thoracic injuries			Treatable sleep disorders appear to be common in sleepy TBI population All 10 had treatable sleep disorders; 3 had symptoms of hypersomnia before inj		Standardized outcomes: 1 Description: 1 Follow-up: 0
Chaput, 2009 Canada	Type: Epi/Prev/Desc Assess the relationships among sleep complaints, headaches, and mood alteration in mTBI	**Level III** Recruitment: Retrospective chart review Consecutive ER Single Group Longitudinal Data retrieval at 10 days and 6 wks Self report: in order to prevent selection bias those pts assessed by self-report and history were not excluded but rated for presence or absence of 6 types of sleep complaints	TBI=443 @ 10 days 87.8% @ 6 weeks 64.1% Inclusion: • Seen for ≥ 1 visit where post-inj symptoms not due to alcohol or other illegal substance, or medication, or other injuries or 2° to treatment of other inj • mTBI diag by neurosurgeon based on task force criteria Exclusion: • ≤ 16 yrs • language barrier • known history of mental retardation, diag of dementia or learning disability impairing the cognitive and reasoning process, or co-existing psychiatric illness	**Age:** mean 46.9 yrs **Gender:** 31.8% F **Severity:** mTBI **GCS:** scene: mean 13.2 (10 day grp) and 15 (6 wk grp) Emergency department: 13.9 and 15 42% abnormal CT-scan **Time since:** <10 days post-trauma and < 6 wks	Review of past medical history including current medications, known allergies as well as smoking, alcohol and drug intake habits CT scans were reviewed if present Rivermead post-concussion symptom assessment questionnaire	Sleep complaint prevalence: 13.3% and 33.5% (sig more likely at 6 wks) Presence of sleep complaints is sig associated with headaches, depressive symptoms and feeling irritable at 10 days and 6 wks Early development of symptoms may increase risk of chronicity of symptoms Appear to indicate an alteration in sleep homeostasis following mTBI despite absence of physical pain as presented at 10 days	Limitations: Did not assess current stressors Subjective nature of data collected	**Moderate:** 3.5 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 0 Standardized outcomes: 0.5 Description: .5 Follow-up: 1

Makley, 2009 USA	Type: Epi/Prev/Desc Investigate whether improvements in sleep efficiency correlate with duration of PTA after closed head injury (CHI)	**Level IVA** Recruitment: Prospective Consecutive AI Single Group Longitudinal Actigraphy within 72 hrs of admission and for duration of stay (min of 7 days) Daily measurement of PTA; cleared when O-LOG score of ≥25 on 2 consecutive days Follow-up at 3 mo	CHI=14 Exclusion: • known history of a sleep disorder, anoxic injury, active psychiatric illness, obesity, untreated thyroid disease, degenerative neurologic condition, sig tetraparesis or immobility	**Age:** 24-45 yrs **Gender**: NI **GCS:** NI **Time since:** 15 days (9-23)	Complete neurologic and physical examination on admission FIM at admission and d/c Actigraphy The Orientation Log (O-LOG) to measure PTA by SLPs blinded to sleep scores Bedside sleep logs kept by nursing staff Follow-up: DRS Supervision Rating Scale SWLS PSQI	78% had mean Week-1 sleep efficiency in the severely impaired range Those admitted having already cleared PTA had sig better Week-1 sleep efficiency than those with ongoing amnesia Those with ongoing amnesia: each 10-unit inc in sleep efficiency correlated with 1 unit ↑ in O-LOG score Association between improvement in sleep efficiency and return of awareness > for those admitted with PTA	Actigraphy a good method to measure sleep patterns in immediate post-acute Strengths: Effort made to measure/eliminate potential confounding variables Limitations: Small sample with large attrition (only 9 available for analysis)	**Moderate:** 3.5 Baseline: 0.5 Blinding: 0.5 Sample size: 0 Attrition: 0 Standardized outcomes: 0.5 Description: 1 Follow-up: 1
Worthington & Melia, 2006 UK	Type Epi/Prev/Desc Investigate the impact of disorders of arousal and sleep disturbance on everyday living and participation in rehabilitation.	**Level V** Recruitment: Retrospective naturalistic observation Recruitment AI (7 centres Cross sectional Single Group	ABI=135 Inclusion: • admission to service on grounds of sig cognitive and/or behaviour disorder • severe BI • all able to participate in rehab Exclusion: NI	**Age:** 38± 11.4 yrs **Gender:** 25% F **GCS:** ranged from 3-7 **Time since:** 119.3± 108.8 mos	Structured rating form: 5 key features - delayed sleep onset, frequent waking at night, early morning waking, delayed morning waking, EDS	47% disturbance of arousal and sleep patterns; Sig adverse effect on activity in 66% of 47% Disordered arousal could persist up to 10 yrs post-inj Concurrent psychiatric illness, but not epilepsy, was associated with arousal and	Strengths: 1st sizeable study to address the impact and management of arousal disorders after BI	**Moderate:** 3/7 Baseline: 0.5 Blinding: 0 Sample size:1 Attrition: 1 Standardized outcomes: 0 Description: .5

						sleep disorder Non-pharmacological interventions used in 34% of cases; benzodiazepine/ hypnotic drugs 20% Long term outcome from sBI affected by enduring disturbance of arousal, most commonly noted as sleep disorder		Follow-up: 0
Reference	**Study Objective**	**Research Design**	**Sample Size Inclusion/ Exclusion**	**Subjects**	**Data Collection Methods/ Measures**	**Significant Findings**	**Comments**	**Quality**
Pathophysiology								
Ayalon et al., 2007 US	Type Pathophysiology Describe the physiologic and behavioural characteristics of circadian rhythm sleep disorders (CRSD) following mTBI in pts complaining of insomnia	Level **III** Recruitment: LC Descriptive Cohort Cross sectional Data collection every 2 hrs for 24 hrs	TBI=42	**Age: m**ean 26 yrs (17-45 yrs) **Gender:** 20% F **GCS:** mTBI **Time since:** NI	Actigraphy Saliva melatonin Oral temperature PSG Self report questionnaire to determine circadian preference: morningness-eveningness questionnaire	36% had CRSD 19% had DSPS: showed ↑temp, rhythm, amplitude 17% had irregular sleep-wake pattern (ISWP): had weaker circadian rhythmicity – account for behaviour differences in sleep-wake pattern? Distinct profiles of 24-hr periodicity of melatonin rhythm and 24-hr periodicity of oral temperature	mTBI might contribute to emergence of CRSD Important to have correct diag or can inappropriately treat for insomnia	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

Baumann et al., 2005 Switzerland	Type Pathophysiology Assess the CSF hypocretin-1 levels in pts with TBI	Level **III** Recruitment: Consecutive A Cohort Cross sectional Data collection 1-4 days post TBI	TBI = 44 C= 20 (no neurologic problems) Inclusion: • Acute TBI, 1-4 days post inj Exclusion: NI	**Age:** mean 36 yrs (17-69 yrs) **Gender:** 73% F **GCS:** 31 sTBI; 8 mod TBI; 5 mTBI **Time since:** 1-4 days	TBI:Hypocretin-1 levels assessed ventricular CSF (N=37) and spinal CSF (N=8) by radioimmunoassay C: levels assessed via spinal anaesthesia and some ventricular Used Marshall to categorize the CT	Hypocretin-1 levels abnormally low in 95% of mod-s TBI and in 97% of those with post-traumatic brain CT changes Site of CSF sample not matter Marshall I: 8; II-IV: 36 N=9 concomitant diseases	Change in levels may reflect hypothalamic damage and may be linked to SWD May also reflect loss of consciousness Limitations: Small sample size	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Quinto et al., 2000 US	Type Pathophysiology Describe the experience of Delayed Sleep Phase Syndrome (DSPS) in ABI	**Level IVA** Recruitment: LC Single Subject Case Study	TBI = 1 Sleep onset insomnia: not responsive to pharmacological treatment	**Age:** 48 yrs **Gender:** male **GCS**: NI **Time since:** NI	Sleep logs Actigraphy	Sleep onset insomnia with frequent awakenings Chronotherapy unsuccessful declined Phototherapy declined	Authors hypothesize lesion to suprachiasmatic nucleus (SCN) which is the site of human circadian clock Emphasized need to be aware of DSPS as a potential consequence of ABI when diagnosing sleep problems	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0

Reference	Study Objective	Research Design	Sample Size Inclusion/ Exclusion	Subjects	Data Collection Methods/ Measures	Significant Findings	Comments	Quality
Paediatric								
Beebe et al., 2007 US	Type Paediatric Determine the effect of mod and severe TBI on sleep of school-aged children	**Level III** Recruitment: Concurrent prospective cohort A (children aged 6-12 yrs) Longitudinal 3 grps: modTBI, sTBI, orthopaedic inj Baseline (Retrospective parental report of pre-inj sleep at 3 wks post), 6, 12, and 48 mos post-inj	mod TBI = 56 sTBI = 53 C= 80 Inclusion: • 1 night in hospital for all 3 grps • No evidence of abuse or previous neurological disorder • English-speaking	**Age:** @ inj 9.5±2.0 yrs **Gender:** 33% F **GCS:** used lowest post-resuscitation/ inj score **Time since:** 3 wks post **Other:** 68% Caucasian	Child Behaviour Checklist: 7 items only (assessed stability in comparison to full scale)	mod TBI worse pre-injury sleep mod TBI and C: small ↓ in sleep from pre to post sTBI: ↑ in post-injury problems: daytime sleepiness and nocturnal sleep duration	Limitations: Timing of follow ups varied Retrospective data collection Weak instrument (only 7 items and part of larger scale)	**Moderate:** 4.5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 0 Standardized outcomes: 0.5 Description: 1 Follow-up: 1
Kaufman et al., 2001 Israel	Type Paediatric Subj and obj characterize the long term effects of mild head injury (mHI) on sleep in adolescents	**Level III** Recruitment: Prospective cohort A(archives) Cross sectional mHI: subj and obj measures C1, C2: obj only C1, C2 matched for age, gender; recruited by advertisement, word of mouth	mHI = 19 C1 (healthy) = 16 C2 (healthy) = 15 Inclusion: • 10-18 yrs • Hospital admission with mHI (ICD-10 codes) • GCS≥13 • 3 yrs post inj • Complained of sleep disturbance Exclusion: NI	**Age:** 13.5 ± 1.7 **Gender**: mHI 21%F; C1 19%F C2 20%F **GCS:** ≥13 **Time since:** 3 yrs post inj	Locally developed questionnaire: medical history, details of the inj, sleep habits, and sleep disturbances: pre and post sleep PSG (mHI and C1): 1 night Actigraphy (mHI and C2): 5 days within 3 mo of PSG	mHI: sig ↓ in sleep period time, total sleep time and sleep efficiency mHI: sig ↑ mins awake and number of awakenings > 3 mins mHI: subj report difficulty falling asleep, difficulty waking in the morning, daytime sleepiness, restless sleep,	Strengths: Thorough evaluation Use of healthy controls Subj corroborated obj for the most part Participants 3 yrs post inj so identifies/confirms long term sleep problems Limitations: Small N but reflective of the realities of this type of research	**Moderate:** 3.5/7 Baseline: 1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: .5 Description: 1 Follow-up: 0

		One data collection, including 5 days of actigraphy				fearful wakenings from sleep, parasomnias		
Milroy et al., 2007 UK	Type Paediatric Obtain obj and subj reports of sleep disturbances in school-aged children with mTBI	**Level III** Recruitment: A (from database) Cross sectional 2 grps: mTBI and orthopaedic controls with inj to wrist or arm	mTBI = 18 (43% of admissions) C = 30 (61% of admissions) Inclusion: • 7-12 yrs • ≥ 6 mos since last hospital attendance • Admission < 48 hrs Exclusion: • Developmental delay, epilepsy, psychiatric, or sleep disorders • Attends a special school • Other recent hospitalization • History of non-accidental inj •	**Age:** mean TBI:9.7±1.5 yrs; C: 9.7±1.5 yrs **Gender:** TBI 56%F, C 40% F **GCS:** GCS of 15 = 16 GCS of 13 = 1 GCS of 14 =1 2% recorded PTA **Time since:** mean TBI 23.9 mos; C 25 mos	Actigraphy for 5 nights Parental and self report questionnaires: Children's Sleep Habits Self-Report Sleep Scale Strengths and Difficulties Demographic and injury-related questions	mTBI: Parents report > sleep disturbances when compared to C (medium effect size) mTBI and C: did not differ on measures of sleep efficiency	Higher proportion in both grps with sleep difficulties than expected Differences between parental report and obj measures of interest as these measures serve different purposes and may identify different types of sleep difficulties Self selection bias possible	**Moderate**: 4/7 Baseline:1 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Necajauskaite et al., 2005 Lithuania	Type Paediatric Investigate the clinical features and prevalence of symptoms of PCS in children with mTBI and evaluate changes over time	**Level III** Recruitment: A Cross sectional Two grps: TBI: single mTBI; C: mild body injury 2 questionnaires mailed separately: 1st for period during	TBI= 102 C = 102 Grps matched on gender, age, date of admission	**Age:** 4-16 yrs **Gender:** 28% F **GCS:** NI **Time since:** 1-5 yrs post admission	Locally develop standardized questionnaire addressing: health and symptoms (irritability, fears, sleep disorders, learning problems, concentration problems, memory disorders, headaches and concomitant symptoms prior to trauma)	16.7% of parents reported sleep problems shortly after head trauma	Limitations: Criteria measured here not reliable estimates of long-lasting PCS Weak measures Only 1 data collection from C Retrospective; possible issues of recall bias	**Moderate:** 3.5/7 Baseline: 1 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 0 Description: .5

		the last yr and during the last mo with no ref to trauma (to reduce bias); 2nd (just TBI grp) for period shortly after the trauma Compared those <2 yrs post inj to those 2-5 yrs post inj						Follow-up: 0
Korinthenberg et al., 2004 Germany	Type: Paediatric Investigate predictive factors of post traumatic syndrome in children with mHI	**Level III** Recruitment Prospective cohort Consecutive A (used specific criteria) Longitudinal Obj and subj measures Data collection: baseline and follow up at 4-6 wks	mHI= 98 Inclusion: • LOC < 10 or none • Able to answer questions at admission • No complications, confusion, or intracranial haemorrhage • Age 3-13 yrs • Child and parents speak German, parent available for interview Exclusion: NI	**Age:** 3-5 yrs=26, 6-9=42, 10-13=30 **Gender:** 40% F **GCS:** NI **Time since:** < 24 hr since admission	EEG Protocol of "examination of child with minor neurological dysfunction" Structured validated interview	At follow up: 23% presented with somatic and psychiatric complaints including sleep disturbance and fatigue, which did not correlate with somatic, neurologic or EEG findings immediately post-inj	Strengths: Large sample size Thorough investigation with follow up Limitations: Better with a further follow up	**Moderate:** 5/7 Baseline: 0.5 Blinding: 0 Sample size: 1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0.5
Pillar et al., 2003 Israel	Type: Paediatric Assess the prevalence and risk factors of long term sleep disturbances in adolescents after mHI	**Level III** Recruitment: Retrospective cohort A ("random" selection from archives) Cross sectional Matched controlled	mHI=98 C=80 Inclusion: • 7-15 yrs at inj • Admitted to hospital with mHI • ICD-10 codes 506.0 • GCS ≥13 on admission et ER Exclusion: NI	**Age:** 8-18; 13.5±2.3 yrs **Gender:** 32% F **GCS:** 14.7±0.6 on admission **Time since:** 0.5-6 yrs	Detailed 60-item questionnaire	mHI: 28% had sleep problems (vs C 11% - p<0.05) mHI > C: average score of sleep complaints (p<0.05) mHI with sleep complaints (N=27) had > body	Strengths: Large sample size Comprehensive questionnaire Large range post-inj Comparison group Limitations: 2/3 response rate	**Low:** 2.5/7 Baseline: 1 Blinding: 0 Sample size:1 Attrition: 0 Standardized outcomes: 0

		comparison group (healthy)				weight, > BMI, parents less educated, ↑ bruxism, shorter weekend sleep time	No information on BMI @ time of inj	Description: .5 Follow-up: 0
Reference	**Study Objective**	**Research Design**	**Sample Size Inclusion/ Exclusion**	**Subjects**	**Data Collection Methods/ Measures**	**Significant Findings**	**Comments**	**Quality**
Neuropsychology								
Mahmood et al., 2004 US	Type Neuropsychology Examine the relationship between sleep disturbances and neurocognitive ability post TBI	**Level IVA** Recruitment: Consecutive AI (archival records) Correlational Cross sectional	TBI = 87 Inclusion: • TBI diag based on medical exam, recovery to post-acute phase, medically determined need for rehab, cognitive function at Level VI (Levels of Cognitive Function Scale) • indication of at least a concussion (LOC or confusion or positive neuroimaging) Exclusion: NI	**Age:** NI **Gender:** 43.7% F **GCS:** mild: 24; mod 19; sev 44 **Time since:** 97% within a year of injury; 89.7% within 6 mo; 70.1% within 3 mo	PSQI BDI Global scale from Memory Assessment Scales Neuropsychology tests: Wide-range Achievement test (WRAT-3) – estimate of pre morbid IQ Digit Span Digit Symbol Grooved Peg Board Block Design Trail making-B Controlled Oral Word Association Test (COWAT)	37% had sleep disturbances mTBI more sleep disturbed than severe Performance on selected measures of cognitive function ↑ prediction of sleep disturbance accounting for 14% of variance beyond that accounted for by inj severity and gender (17%) executive functioning and speed of information processing difficulties may be associated with sleep disturbances	PSQI better at identifying insomnia but may have not have captured hypersomnia Need a reliable indicator better able to detect and report sleep disturbances Need to further assess the influence of gender; explore the threshold level and changes over time	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size:1 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Wilde et al., 2007 US	Type Neuropsychology Examine the impact of	**Level III** Recruitment: PA (3 centres, sleep disorder	TBI = 35: OSA = 19 No OSA=16	**Age:** > 18 yrs **Gender:** OSA: 11%F No OSA: 25%F	Neuropsychological performance: Psychomotor Vigilance test Rey Complex	OSA ↓ on verbal and visual delayed-recall measures and > attention lapses	Strengths: First study to address this issue	**Moderate:** 4/7 Baseline: 1

	comorbid OSA on cognitive function of persons with TBI	centres and a rehab prog) Case controlled Cross sectional 2 TBI grps: OSA and No OSA Controlled using age, education, time post inj, and severity of inj and GCS (when avail) OSA diagnosed by nocturnal PSG	Inclusion: • > 18 yrs • ≥ 3 mos post-inj Exclusion: NI	**GCS:** OSA 53% unknown, 16% mod, 5% mod-sev, 26% sev No OSA: 50% unknown, 12% mod, 19% mod-sev, 19% sev **Time since:** ≥ 3 mos post-inj	Figure Rey Auditory-Verbal Learning Digit Span from WMS-R Finger tapping ESS on night of PSG and MSLT	Effect sizes using Cohen d: were medium and large	OSA associated with more impairment of sustained attention and memory Treatment of OSA did not improve outcomes Limitations: Lacked data on levels of severity, difficult to generalize findings Small N but effect sizes good	Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 0
Wiseman-Hakes et al., 2010 Canada	Type: Neuropsychology Assess aspects of cognition and communication over a course of treatment for post traumatic hypersomnia (PTH)	**Level IVA** Recruitment: LC Single case study Treatment: 17 wks 1. Baseline: 12 mo post inj - Lorazepam 1 mg and Citalopram 20mg for 1 mo 2. At 1 yr1mo : Citalopram ↑40mg 3. At 1 yr2mo: add Ritalin 20mgs 4. At ↑40mg daily 5. Sleep Study 2: modafinil replace Ritalin and mirtazepine was	TBI= 1	**Age:** late teens **Gender:** male **GCS:** initial 3, hospital 5 PTA > 1 mo **Time since:** 11 mos	Daily Cognitive-communication and Sleep Profile (D-CCASP) ESS Stanford Sleepiness Scale PSG Maintenance of Wakefulness Testing (MWT) (at follow up)	Relationship between quality of sleep and language processing Prolonged REM latency Positive relationship between sleep and language processing, sustained attention/vigilance, memory and changes in medication Able to improve daily functioning and resume attendance at school	Limits: Single case study and exploratory in nature	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 0.5 Description: 1 Follow-up: 1

		added Baseline, 17 wks daily data collection, follow up at 3 yrs 8 mos						
Henry et al., 2000 US	Type Neuropsychology To Investigate neuropsychological, psychological and behavioural functioning following non-impact BI	**Level V** Recruitment: Retrospective OR Cross sectional Interviewed at one point in time Compared with published norms	Non-impact TBI=32 Inclusion: • History of whiplash with brief or no LOC and no evid of cranial trauma • No physical evid that head struck windshield/headrest • Subj report of an alteration in mental status at accident with no obj evid Exclusion: • Previous whiplash or closed BI, neurological disorder, seizure, psychiatric problem, substance abuse or medical condition or medication that compromise nervous system integrity	**Age:** 18-64; mean 41.8 yrs **Gender:** 53% F **GCS:** NI **Time since:** 1 wk to 5 yrs	Clinical interviews corroborated via interviews with significant others/ coworkers Neuropsychology battery: Wechsler Adult Intelligence Scale – revised (WAIS-R), WMS-R, Rey figures, Hooper, Boston naming and verbal fluency, Trials A and B, Wisconsin Card Sort, Strop, auditory consonant trigrams, PASAT	Cognitive deficits observed particularly with executive functioning (attention and concentration) PASAT most sensitive test Some experience of mild depression Problems observed with behavioural control, sleep and sexuality EEQ showed front-central slowing and ↑ in spike activity	Whiplash can produce wide-ranging circuitry dysfunction (similar to mTBI)	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 0 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: .5 Follow-up: 0

Reference	Study Objective	Research Design	Sample Size Inclusion/ Exclusion	Subjects	Data Collection Methods/ Measures	Significant Findings	Comments	Quality
Intervention								
Jha et al., 2008 US	Type Intervention Test the efficacy of modafinil in treating fatigue and EDS	**Level II** **Downs and Black:** 23/28 Recruitment: PA double blind, placebo-controlled crossover trial: 4 wk washout period, 4 wk open label trial at end modafinil: 2 x 100 mg twice a day for 8 wks with 2 wk graduated in (manufacturer provided) data collection: baseline, week 4, week 10, weeks 4 and 10 after crossover	E1 = 24 (drug first) E2 = 22 (placebo first) Inclusion: • 1 yr post-TBI (severe enough to require inpt rehab) • 18-65 yrs • Report fatigue and/or EDS compromising functioning Exclusion: • neurologic/neuron psychiatric diag • Other diag for EDS • Concurrent sig systemic disease • Epilepsy • Cardiovascular disease • Sig psychiatric or behaviour symptoms • Non-English • Pregnant females or potential child-bearing unless using contraceptives	Age 38.25(12.20) **Gender:** 31.4% F **GCS:** severe: 3-8 (51%); moderate 9-12 (23.5%); mild 13-25 (25.5%); **Time since:** 5.77±4.97 yrs	Modified Fatigue Impact Scale Fatigue Severity Scale ESS MOS-12 item SF-12 Post Concussion Assessment Cognitive Testing (Impact) Connor's continuous performance test II BDI II	ESS: E1>E2 at week 4 but not at week 10: only short term beneficial Insomnia reported more often with drug than placebo Safe and well-tolerated There was no sig differences between modafinil and placebo and no consistent and persistent clinically sig differences	Strengths: Thorough complete information with demographics, methodology Acknowledged complexity of fatigue and relationship with sleepiness Limitations: All sleep measures self-report Standard dosage therefore not able to tailor to individual (modify to meet individual responses (ex. taper) Single center Multiple stat tests, Clinical sig complicated as most did open label	**High:** 6.5/7 Baseline: 1 Blinding: 1 Sample size: .5 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 1
Castriotta, 2008 USA	Type Intervention Determine	**Level III** **Downs and Black:** 17/28	TBI = 57 Inclusion: • > 18 yrs	**Age:** 38.6 ±14.8 yrs **Gender:** 25% F	Sleep : NPSG MSLT ESS	39% had abnormal sleep studies :23% OSA, 3% PTH,	Strengths: Rigorous methods; used established	**Moderate**: 5/7 Baseline: 1

	whether treatment of sleep disorders identified in BI adults results in resolution of those disorders and improvement of symptoms and daytime function	Recruitment: Prospective unselected pts AI (3 centres) Longitudinal Baseline and 3 mos; neuropsychological testing performed at 10:30 to control for diurnal variation; only those with sleep disorder did the sleep assessment again at 3 mos	• ≥ 3 mo post inj Exclusion: • Presence of circadian rhythm disorder • Unable to give informed consent • Use of sedating medications	**GCS:** used with CT findings according to criteria to establish severity 30% sTBI; 5% mod-sTBI; 18% mod TBI; 9% mTBI; 38% missing **Time since:** 67.8 ±126.3 mo	Neuropsychological : PVT POMS FOSQ Urine sample to test for drugs/medications Treatment : CPAP for OSA Modafinil for narcolepsy and PTH Pramipexole for Periodic Limb Movement Syndrome (PLMS)	5% narcolepsy, 7% PLMS 21% EDS GCS ↓ for sleep disordered Sleep disordered > reductions in tension and anger and ESS than non-disordered Apnea/hypopnea Index improved with treatment ↑ Amount of REM Treatment may result in NPG resolution without change in sleepiness of neuropsychological function	criteria as much as possible Limitations: Medications not titrated Large missing severity data Subsamples small MSLT not the right measure as it seems that sleep and wakefulness are 2 separate active processes	Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 1
Francisco & Ivanhoe, 1996 US	Type: Intervention Effects of methylphenidate on post traumatic narcolepsy	**Level IVA Downs and Black:** 11/28 Recruitment: LC Single Case Study Methylphenidate: 10mg 2x/day then ↑ to 30mg 2x/day over 4 mos	TBI=1 Classic tetrad of narcolepsy (cataplexy, EDS, sleep paralysis, hypnogogic hallucinations); diag confirmed by PSG and MSLT No structural, metabolic, or cardiac abnormalities that explain the symptoms	**Age:** 27 yrs **Gender:** Male **GCS:** 3 at inj site but 7 at ED; mod TBI **Time since:** 22 mo	PSG MSLT	1 mo after initiation cataplexy and EDS started to improve 6 mo after the start of treatment the pt is asymptomatic At 12 mo medications was involuntarily withdrawn and symptoms returned	Drugs leading to norepinephrine release may be helpful in reversing the symptoms of narcolepsy	**Moderate:** 4.5/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: 1 Follow-up: 1

Ouellet & Morin, 2007 Canada	Type Intervention Determine the efficacy of cognitive behaviour therapy (CBT) in TBI	**Level III** **Downs and Black:** 16/28 Recruitment: OR Single case design with multiple baselines across subjects 8-wk CBT addressing stimulus control, sleep restriction, cog restructuring, sleep hygiene, education and fatigue management Sleep diary for 2 wks at follow up and baseline, 3 , 5 or 7 wks randomly determined across subgrps of 3 1 and 3 mo follow up	TBI = 11 Inclusion: • 18-50 yrs • TBI in last 5 yrs • Not an inpt • Insomnia syndrome (operational definition) • If on meds for 6 mos and stable Exclusion: • Major untreated or unstable medical or psychiatric co-morbidity • Meds known to prod insomnia • Sleep disturbances before TBI • Another sleep disorder • Unable to complete questionnaire • Experience sig pain	**Age:** 27.3 yrs **Gender:** 46% F **GCS:** 3-14; 2 no data; m to sTBI as evaluated by multidisciplinary team using standard criteria **Time since:** 25.64 mos	Sleep diary (Total wake time, Sleep efficiency) Diagnostic Interview for Insomnia ISI MFI Dysfunctional Beliefs and Attitudes about Sleep Scale BDI BAI 2 night PSG Short telephone interview at follow-up by independent interviewer	Baseline results showed variability as expected Clinical and sig reductions in total wake time and sleep efficiency for 8/11 (74%) Prog generally well maintained at follow-up Sleep efficiency augmented ↓ fatigue symptoms	Strengths: Good baseline table CBT seems promising Limitations: Needed to include description of CBT Did not assess cognitive functioning Women were over-represented Self-selected so may be more motivated to change.	**Moderate**: 4.5/7 Baseline: 0.5 Blinding: 0.5 Sample size: 0 Attrition: 1 Standardized outcomes: 1 Description: .5 Follow-up: 1
Ouellet & Morin 2004 Canada	Type Intervention To test the efficacy of CBT for insomnia with TBI in a person with difficultly falling asleep and staying asleep since inj	**Level III** **Downs and Black:** 10/28 Recruitment: OR Single case study 8 wkly individual manualized CBT	N = 1 Diagnostic clinical interview determined that had mixed insomnia (ICSD and DSM)	**Age:** late 30s **Gender:** male **GCS:** 13/15, no coma, PTA 5-7 days, moderate TBI **Time since:** NI	Sleep diary for 5 wks of baseline 8 wks CBT, 2 wk post treatment and follow up at 1 and 3 mos PSG (5 nights: 3 pre and 2 post) Insomnia Severity Index (ISI) Dysfunctional Beliefs and	Sleep onset ↓ from 47 minutes to 18 and nocturnal awakenings ↓ from 85 to 28 minutes; both below clinical criteria Sleep efficiency ↑ from 58% to 83%	Strengths: Was adapted for TBI The behavioural recommendations in the intervention were simple and straight forward Promise for non-	**Moderate:** 4/7 Baseline: 0.5 Blinding: 0 Sample size: 0 Attrition: 1

		sessions (adapted for TBI) addressing stimulus control, sleep restriction, cog restructuring and sleep hygiene education given by a clinical psychologist 5 wks of baseline, 8 wks CBT, 2 wk post treatment and follow up at 1 and 3 mos			Attitudes about Sleep Scale MFI BAI	PSG corroborated data Majority of gains were maintained at follow up (tapering of med was occurring) ISI dropped from clinical to sub-clinical score	pharmacological interventions, particularly CBT	Standardized outcomes: 0.5 Description: 1 Follow-up: 1
Shan & Ashworth, 2004 Canada	Type Intervention Assess the effects of lorazepam versus zopiclone on cognition	**Level II** **Downs and Black:** 23/28 Recruitment: Consecutive AI Double blind, crossover trial Self regulate (0, ½, or full tablet) of lorazepam (.5-1.0 mg) or zopiclone (3.75-7.5 mg) at bedtime for 7 days Starting dose randomly generated At 2 wks state which intervention prefer	ABI and stroke = 18 (ABI: 6) E1=9 E2=9 Inclusion: • > 18 yrs • Secondary causes of insomnia OK: depression, apnea, restless legs Exclusion: • acutely ill • Non-English/French • Unable to read questions • Severe cognitive impairment	**Age:** 56.6 yrs **Gender:** 44% F **GCS:** NI **Time since:** NI	Folstein MMSE: baseline, during week 1 and week 2 Rate quality of sleep from night before (2 of 7 days but not the first 3 days) – locally developed Total sleep time recorded by nursing staff q 30 mins or 1 hr Nurses rated restfulness and drowsiness on a 1-4 scale Testing for ataxia	The medications seem to be equally effective	Limitations: Non-pharmacological interventions used Criteria participants used for self dosing not clear Weak measures: locally developed as convenience, thought more sensitive than Morning Sleep Questionnaire and no gold standard Excluded severe impairment	**Moderate:** 3.5/7 Baseline: 0.5 Blinding: 1 Sample size: 0 Attrition: 1 Standardized outcomes: 0 Description: 1 Follow-up: 0

Appendix B

University of Toronto Research Ethics Board Approval

University of Toronto
Office of the Vice-President, Research

Office of Research Ethics

PROTOCOL REFERENCE #23867

February 26, 2009

Dr. Angela Colantonio
Rehabilitation Sciences
500 University Ave.
Toronto, ON M5G 1V7

Ms. Catherine Wiseman-Hakes
Rehabilitation Science
640 Broadway Ave.
Toronto, ON M4G 2S7

Dear Dr. Colantonio and Ms. Wiseman-Hakes:

Re: Your research protocol entitled "Sleep/Wake disorders following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance"

ETHICS APPROVAL	**Original Approval Date: February 26, 2009** **Expiry Date: February 25, 2010** **Continuing Review Level: 1**

We are writing to advise you that a member of the Health Sciences Research Ethics Board has granted approval to the above-named research study, for a period of **one year**, under the REB's expedited review process. Ongoing projects must be renewed prior to the expiry date.

The following consent documents (received February 26, 2009) have been approved for use in this study:
Information Letter
Informed Consent

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events should be reported to the Office of Research Ethics as soon as possible.

Please ensure that you submit an Annual Renewal Form or a Study Completion Report at least 30 days prior to the expiry date of your study.

Best wishes for the successful completion of your project.

Yours sincerely,

Daniel Gyewu
Research Ethics Coordinator

McMurrich Building, 12 Queen's Park Cres. W, 3rd Floor Toronto, ON M5S 1S8
TEL: 416-946-3273 FAX: 416- 946-5763 EMAIL: ethics.review@utoronto.ca

Appendix C

Sunnybrook Health Sciences Centre Research Ethics Board Approval

Sunnybrook
HEALTH SCIENCES CENTRE

Research Ethics Office, Room C819
2075 Bayview Avenue
Toronto, ON Canada M4N 3M5
t: 416-480-6100 ext. 4276 or 88144
http://sunnybrook.ca/research/?page=reohome

MEMORANDUM

To: Dr. Brian Murray
Neurology
Room M1 600

From: Dr. Philip Hébert

Date: June 5, 2009

Subject: **Sleep/Wake Disorders Post Traumatic Brain Injury; Impact on Recovery of Cognitive-Communication Performance**

Project Identification Number: 109-2009
Approval Date: June 5, 2009

The Research Ethics Board of Sunnybrook Health Sciences Centre has conducted a Delegated Board review of the research protocol referenced above and approved the involvement of human subjects as specified in the protocol on the above captioned date. The quorum for approval did not involve any member associated with this project.

The approval of this study includes the following documents:

- Protocol dated December 2008
- Informed Consent Form dated May 2009
- Clinician Information Letter
- Information Letter
- Telephone Script: Prospective Participants dated January 2009
- La Trobe Communication Questionnaire
- Daily Cognitive Communication and Sleep Profile (D-CCASP)
- Diagnostic Interview for Insomnia
- Insomnia Severity Index (ISI)
- Beck Depression Inventory: Mood Related Questions

The above Project Identification Number has been assigned to your project. Please use this number on all future correspondence.

Should your study continue for more than one year you must request a renewal on or before one year from the approval date. Please advise the Board of the progress of your research annually and/or any adverse reactions or deviations which may occur in the future.

Approval of this study by the Sunnybrook REB entails that this study complies with current legislation as outlined in the Ontario Personal Health Information Protection Act (PHIPA) and all policies and guidelines established by Sunnybrook Health Sciences Centre. All applicable contracts and agreements must be submitted to Sunnybrook Research Administration before this research may be initiated.

Philip C. Hébert, MD PhD FCFPC
Chair, Research Ethics Board
/tt

Appendix D

University Health Network Notification of REB Initial Approval

University Health Network
Toronto General Toronto Western Princess Margaret

University Health Network
Research Ethics Board
8th Floor South, Room 8-23
700 University Ave
Toronto, Ontario, M5G 1Z5
Phone: (416)946-4438

Notification of REB Initial Approval

Date: September 1st, 2009
To: Dr. Chanth Seyone
7th Floor, Room 427, Main Pavilion, Toronto Western Hospital
399 Bathurst St.
Toronto, Ontario, Canada
M5T 2S8

Re: 09-0423-BE
Sleep/Wake Disorders Following Moderate-Severe Traumatic Brain Injury; Impact on Recovery of Cognitive-Communication Performance

REB Review Type:	Expedited
REB Initial Approval Date:	September 1st, 2009
REB Expiry Date:	September 1st, 2010

Documents Approved:

Protocol	Version date: June, 2009
Consent Form - Participant	Version date: August 24th, 2009
Consent Form - Sleep Observer/Communication Partner	Version date: August 24th, 2009
Daily Cognitive Communication and Sleep Profile	Version date: 2008
Clinician Referral Form	Version date: September 1st, 2009
Telephone Script	Version date: January, 2009
Clinician Information Letter	Received on: June 9th, 2009
Information Letter	Version date: August 28th, 2009

The above named study has been reviewed and approved by the University Health Network Research Ethics Board. If, during the course of the research, there are any serious adverse events, confidentiality concerns, changes in the approved project, or any new information that must be considered with respect to the project, these should be brought to the immediate attention of the REB. In the event of a privacy breach, you are responsible for reporting the breach to the UHN REB and the UHN Corporate Privacy Office (in accordance with Ontario health privacy legislation - Personal Health Information Protection Act, 2004). Additionally, the UHN REB requires reports of inappropriate/unauthorized use of the information.

Please be aware that it is UHN policy that research-related activities involving an external party require a research agreement. An 'external party' refers to a corporation other than UHN or an individual who is not UHN personnel. Should a research agreement be required in this case, the study may not begin at UHN until the agreement has been signed by all parties. Should the negotiation process raise concerns, the REB reserves the right to reconsider its approval.

If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The REB must be notified of the completion or termination of this study and a final report provided. As the Principal Investigator, you are responsible for the ethical conduct of this study.

The UHN Research Ethics Board operates in compliance with the Tri-Council Policy Statement, ICH/GCP Guidelines, the Ontario Personal Health Information Protection Act (2004), and Part C, Division 5 of the Food and Drug Regulations of Health Canada.

Sincerely,

Ronald Heslegrave, Ph.D.
Chair, University Health Network Research Ethics Board

Appendix E

West Park Cullen: Final Approval

Notification of JREB Approval

December 20, 2010

Dr. Nora Cullen (c/o Catherine Wiseman-Hakes)
West Park Healthcare Centre
84 Buttonwood Ave.
Toronto, ON
M6M 2J5

Study Title	Sleep/wake disorders following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance
REB Review Type	EXPEDITED REVIEW
REB Amendment Approval Date	N/A
REB Approval Date	December 20, 2010
REB Expiry Date	December 20, 2011
Documents Approved	JREB Application Form, Study Protocol (Version dated November 2009), Appendix A (Version dated November 2009), Appendix B (Version dated November 2009), Telephone Script (Version dated January 2009), Information Letter (Version dated 2009), Informed Consent Form (Version dated August 10, 2009), Clinician Information Letter

Dear Dr. Cullen:

I am writing to confirm that your protocol entitled, "Sleep/wake disorders following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance" has received *full ethical approval* and you may proceed with data collection.

If, during the course of the research, there are any serious adverse events, any confidentiality concerns, changes in the approved protocol or consent form, or any new information that must be considered with respect to the project, these should be brought to the immediate attention of the JREB. In the event of a privacy breach, you are responsible for reporting the breach to the JREB (in accordance with Ontario health privacy legislation – Personal Health Information Protection Act, 2004). Additionally, the JREB requires reports of inappropriate/unauthorized use of the information.

The Joint Bridgepoint-West Park-Toronto Central Community Care Access Centre Research Ethics Board (JREB) operates in compliance with the Tri-Council Policy Statement, ICH/GCP Guidelines, the Ontario Personal Health Information Protection Act, and Part C, Division 5 of the Food and Drug Regulations of Health Canada.

Should you wish to make any further changes or revisions to any aspect or portion of the approved project, they must be submitted for consideration to the board prior to amending the protocol. Address any proposed changes to: Joint Research Ethics Board, c/o Dale Min, Bridgepoint Health, 14 St. Matthews Rd., Toronto, ON, M4M 2B5.

Finally, all research conducted at Bridgepoint Health, West Park Healthcare Centre or the Toronto Central Community Care Access Centre is subject to ongoing monitoring that includes the submission, in writing, of an **annual** status report of project activities to the board. If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The JREB must be notified of the completion or termination of this study and a final report provided. As the Principal Investigator, you are responsible for the ethical conduct of this study.

Best wishes for the progress of this work.

Yours very truly,

Ron Heslegrave, PhD
Chair, Joint Bridgepoint / West Park / Toronto Central CCAC Research Ethics Board

Appendix F

Toronto Rehab Institute Approval

Toronto Rehab
Everything Humanly Possible

December 7, 2009

Dr. Nora Cullen
Toronto Rehabilitation Institute - University Centre
550 University Avenue
Toronto, Ontario
M5G 2A2

Dear Dr. Cullen:

RE: TRI REB # 09-038
Sleep/wake disorders following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance

The Toronto Rehabilitation Institute Research Ethics Board has reviewed the above-named submission. Any concerns and requested revisions have been addressed to the satisfaction of the REB. The protocol (version date November 2009) is approved for use for the next 12 months. If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The REB must also be notified of the completion or termination of this study and a final report provided. The following documents have also been approved for use as part of this study:

- Clinician Information Letter (as received on October 27, 2009)
- Informed Consent Form: Participant (version date October 24, 2009)
- Informed Consent Form: Sleep Observer and Communication Partner (version date August 10, 2009)
- Clinician Referral form (as received on August 17, 2009)
- Information Letter (as received on August 17, 2009)
- Telephone Script (version date December 2009)

If, during the course of the research, there are any serious adverse events, changes in the approved protocol or consent form or any new information that must be considered with respect to the study, these should be brought to the immediate attention of the Board.

Best wishes for the successful completion of your project.

Yours sincerely,

[ ] Gaétan Tardif MD FRCPC
Chair, Research Ethics Board
Toronto Rehabilitation Institute

[ ] Ann Heesters BEd, BA, MA, PhD(ABD)
Vice Chair, Research Ethics Board
Toronto Rehabilitation Institute

December 7, 2009
Date of Initial REB Approval

December 7, 2010
Expiry Date of REB Approval

TRI REB conforms with the *Tri-Council Policy Statement Ethical Conduct for Research Involving Humans* and Ontario Privacy Legislation *PHIPA*

Toronto Rehabilitation Institute
A University of Toronto Teaching and Research Hospital

University Centre
550 University Avenue
Toronto, Ontario M5G 2A2

Tel: 416-597-3422
www.torontorehab.com

Appendix G

Clinician Information Letter

Clinician Information Letter

Study: Sleep/Wake disorders following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance

Investigators: Catherine Wiseman-Hakes PhD candidate, supervisor, Angela Colantonio, PhD.

CONTACT: 416 946-8574 catherinew.hakes@utoronto.ca

Background: Traumatic brain injury (TBI) is a leading cause of disability for those under the age of 45 in North America. Cognitive-communication impairments are common sequelae of TBI, and occur at a frequency of 81% in the acute stage. These include deficits in sustained and complex attention, verbal memory, impaired efficiency and speed of language processing and impairments in new learning. Impairments in sleep patterns and the development of secondary sleep disorders including insomnia, fatigue and excessive day-time sleepiness are among the most commonly reported neuropsychiatric sequelae in the TBI population. Research has shown that sleep plays a major role in cognitive function, memory, consolidation of new learning, and the ability to modulate emotional response to increasingly adverse stimuli. While there is research to support the incidence of sleep disorders after TBI, there is a paucity of research on the topic of sleep and recovery of neuro-cognitive-communication performance post TBI. Further, prior studies are only cross sectional in nature, and with few exceptions, rely exclusively on self reported measures of sleep. There is a paucity of information regarding the relationship between post traumatic sleep disorders and how they affect survivor's abilities to attend to and process language effectively, (which are pre-requisites for verbal memory, new learning and effective participation in rehabilitation and community reintegration).

Purpose: The proposed study aims to advance our understanding of the dynamic nature of sleep in relation to recovery of neuro-cognitive-communication performance (in survivors of TBI) via a longitudinal design, and by using both objective and subjective measures of sleep.

Brief Description: Participants will complete an interview regarding sleep and functional communication. They will undergo baseline testing of cognitive-communication status, and will then complete an overnight sleep study (polysomnography) in a sleep lab and an assessment by a sleep physician. They will be provided with treatment for their sleep (or wake) problem and monitored. When treatment has reached maximum efficacy and sleep has stabilized, (approximately 2 weeks – 2 months, as determined collaboratively between the physician and participant), a re-evaluation of cognitive-communication status will be conducted. Throughout the study, participants will complete a self monitoring profile of their sleep, and day-time cognitive-communication function, on a daily basis.

Funding: This study is generously supported by the Canadian Institutes for Health Research through a Fellowship in Clinical Research.

Sleep/Wake disorders following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance

Contact: Catherine Wiseman – Hakes 416 946-8575 catherinew.hakes@utoronto.ca

Inclusion Criteria: A. (For referral to the study)

- Formal diagnosis of moderate-severe TBI as indicated by one or more of the following;

1. GCS $\leq$ 12
2. PTA $\geq$ 24 hrs
3. Retrograde amnesia
4. Evidence of intracranial bleed
5. Required neurosurgery

- $\geq$ 1 years post injury
- Age 18-55
- Formal documentation of cognitive-communication deficits secondary to TBI, including report of difficulties with attention, following conversation, memory and new learning.
- Ability to speak and read English
- Self report of post traumatic sleep disturbance and or excessive day-time sleepiness due to apnea, restless leg syndrome (RLS) or post traumatic narcolepsy.
- Not currently being treated for a sleep or wake disorder
- Not currently receiving treatment from a speech language pathologist for cognitive-communication impairments (or willing to put treatment on hold for duration of study)
- Can be receiving treatment from an SLP for speech and or swallowing disorders
- Rancho Level 8 (able to cognitively understand the purpose of the study and comply with protocol as best they can)

B. To proceed in the study as determined by the PI.

- Verification of type of sleep complaint by questionnaire Diagnostic Interview for Insomnia (DIA), Appendix A, and polysomnography
- Score of $\geq$15 on the ISI (Insomnia Severity Index)
- Subjects will have agreed to participate as evidenced by their written signed informed consent

Exclusion Criteria

- Behavioural Disturbances, impulsivity
- Pre-injury diagnosis of primary depression, generalized anxiety disorder, or attention deficit disorder
- Active substance abuse
- History of psychosis
- Subjects who have taken Modafinil or Ritalin for 72 hours prior to the baseline assessment or the sleep test
- Cognitive level Rancho 7 or less

Appendix H

Clinician Referral Form

Clinician Referral Form: Date of referral _____

Study: Sleep/Wake Disorders Following Moderate-Severe Traumatic brain Injury; Impact on Recovery of Cognitive-Communication Performance

Name of clinician: _____ Phone number: _____
(Please print)

Relationship to potential participant: _____

My client Mr. /Ms. _____ has been informed of the study "Sleep Wake disorders following traumatic brain injury; Impact on recovery of cognitive-communication performance". This client meets the eligibility criteria and is interested in learning more about the study as a potential participant. I believe they have the cognitive capacity to fully understand and participate in the study. They have given verbal consent to share the following personal health information;

Diagnosis:_____ Date of Injury: _____ Initial GCS _____

Date of Birth: _____ Sex: _____ Length of Coma: _____

Length of PTA: _____ CT scan or MRI Findings

_____
_____
_____

Self report of sleep problems **but not currently being treated** (please indicate if yes) ___

Self or clinician report of attention, processing and memory problems: yes___ no ____

Self or clinician report of difficulties with social communication (following and participating in conversation etc) yes___ no ____

Contact phone number (or email) for client:
_____

Please return to Catherine Wiseman-Hakes, Study coordinator, and principal investigator; at

fax 416 946-8570: with cover letter (attention Dr. Angela Colantonio)
or mail: Graduate Dept of Rehabilitation Science
University of Toronto
Centre for Function and Well Being
500 University Ave rm 160
Toronto, Ont. M5G 1V7

Clinician Referral Form: Wiseman-Hakes 2009

FAX COVER SHEET

Fax to: Dr Angela Colantonio and Catherine Wiseman-Hakes

Fax Number: 416 946- 8570, University of Toronto

Fax From: _____

Contact Phone Number: _____

Comments: Confidential: Study Referral

_____

Number of pages (including cover sheet) _____

Clinician Referral Form: Wiseman-Hakes 2009

Appendix I

Potential Participant Information Letter

INFORMATION LETTER

Sleep/Wake Disturbance Following Traumatic Brain Injury: Impact on Recovery of Cognitive-Communication Performance

Did you have a traumatic brain injury (TBI)? Were you in a coma? Since your injury do you have difficulty sleeping at night, or staying awake during the day?

Do you also have trouble concentrating or staying focused for periods of time, following conversations or remembering things you have done, heard or read? If so, you may be eligible for a research study.

A group of researchers from the University of Toronto are studying the impact of sleep problems on recovery from TBI, specifically in the areas of paying attention and concentrating, language processing (being able to listen to and follow conversation) and verbal memory (remembering information that you have heard, talked about or read).

In this study, everyone will be asked to complete an interview about their sleep and any difficulties they may be having. We will also ask some questions of the bed partner or someone who knows your sleep patterns (if available). Following this, everyone will be asked to see a doctor specializing in sleep problems, and will then have a detailed assessment.

At the same time, everyone will be asked to participate in some testing of their thinking and communication abilities and will also be asked to rate their own communication. After the sleep study, everyone will be offered the appropriate treatment for their sleep problem (by the doctor). Once the treatment has taken effect, (as determined by the doctor and the individual) everyone will be asked to repeat the testing of their thinking and communication abilities.

Throughout the study, everyone will be asked to rate their sleep and their daytime function on a daily basis.

This study will help us to learn more about the impact of sleep and wake problems following TBI on recovery, and may lead to guidelines for the assessment of sleep problems after TBI.

Please note that if you take part in this study, you will not be identified in any way in any reports that come out of our research. All identifying information will be removed.

Information Letter: Wiseman-Hakes 2009

If you are interested in participating in this study, please contact Catherine Wiseman-Hakes, the main researcher and study coordinator at 416 946-8575.

Your participation in this study will help us to get up-to date information regarding the sleep problems of individuals with TBI and how this may affect the recovery of some of their thinking and communication abilities. This information (may/will) be used to inform and guide healthcare professionals about the importance of assessing and treating sleep after brain injury.

Participants will be compensated for their time and costs. Thank-you for your interest!!!!!

Appendix J

University of Toronto Consent to Participate Form

INFORMED CONSENT FORM: PARTICIPANT

TITLE: Sleep Disorders Following Moderate- Severe Traumatic Brain Injury; Impact on Recovery of Cognitive-Communication Performance

INVESTIGATORS:
Ms. Catherine Wiseman-Hakes (PhD student), Contact: 416 946-8575, Catherinew.hakes@utoronto.ca
Dr. Angela Colantonio PhD (OT. reg.) (supervisor)
Dr. Brian Murray, MD FRCP (Sunnybrook Health Sciences Centre)
Dr. Chanth Seyone, MD FRCP (University Health Network Toronto Western)
Dr. Nora Cullen, MD FRCP

SPONSOR: This project is generously supported by a fellowship through the Canadian Institutes for Health Research (CIHR).

This study is being conducted in partial fulfillment of the requirements for the Doctor of Philosophy in Rehabilitation Science, Faculty of Medicine, University of Toronto.

INFORMED CONSENT

You are being asked to consider participating in a research study. A research study is a way of gathering information on a treatment, procedure or medical device or to answer a question about something that is not well understood.

This form explains the purpose of this research study, provides information about the study the tests and procedures involved, possible risks and benefits, and the rights of participants.

Please read this form carefully and ask any questions you may have. You may take as much time as you wish to decide whether or not to participate. Please ask the study staff or one of the investigator(s) to clarify anything you do not understand or would like to know more about. Make sure all your questions are answered to your satisfaction before deciding whether to participate in this research study.

INTRODUCTION

You are being asked to consider participating in this study because you have a traumatic brain injury and some difficulties with your sleep, your thinking and communication.

Why is this study being done?

The purpose of this study is to help us learn more about how sleep and wake problems after traumatic brain injury (TBI) can affect recovery of some aspects of thinking and communication. It is our hope that by advancing our understanding of the relationship between sleep and the recovery of thinking and communication abilities, we may be able to inform and guide healthcare professionals about the importance of assessing and treating sleep after brain injury. Although it is not guaranteed that there will be any immediate benefits to you or other participants, we hope that the knowledge gained will contribute to future care and treatment of people with TBI. Please read this information sheet carefully and take your time to make your decision about whether you would like to participate.

WHAT WILL HAPPEN DURING THIS STUDY?

If you agree to participate, you will come to the University of Toronto for approximately 1 hour for an interview about your sleep, your mood and your communication. Then we would contact your family doctor (or the doctor who suggested that you may be interested in participating in this study) for a referral for a sleep assessment, and we would ask you to begin keeping track of your sleep and your thinking abilities on a daily basis, using a special form. A few weeks later, you would see a doctor specializing in sleep problems and the brain at Sunnybrook Hospital. Around the same time you see the sleep doctor, you would complete a series of neuropsychological and communication tests, to help us understand how you are able to pay attention and concentrate, follow conversations and remember things. This would take about an hour and a half to two hours.

After you have the sleep study, you will be offered treatment by the sleep doctor. You will begin the treatment and continue until you and the doctor feel that it is working. This usually takes anywhere from 2 weeks to 2 months depending on your specific sleep problem. Once your sleep has stabilized/improved, we will repeat the neuropsychological and communication tests. You would continue to keep track of your sleep and thinking skills on a daily basis using the special form until the end of the study. Dr. Wiseman-Hakes/Colantonio will cover the costs of your treatment for as long as you are in the study where not otherwise covered.

This study also involves accessing some of your medical records to obtain background information relevant to the study (for example, the details surrounding your injury, MRI or CT scans, or results of neurological or cognitive-communication tests or neuropsychological exams). This information will remain confidential and will only be accessible to the investigators during the course of the study.

This study also involves having a family member of yours come to the University of Toronto and answer a number of questionnaires about your sleep and communication. This is done so that we have a good estimate of your sleep and communication from the perspective of someone who knows you well.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

It is anticipated that about 30 people will participate in this study. All participants will have their sleep assessed and treated at Sunnybrook. The length of this study for participants is approximately 2-3 months, depending on how long it takes for your sleep to improve as determined by you and the doctor who will treat your sleep problem. The entire study is expected to take about 2 years to complete.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you decide to participate in this study you will be asked to do the following:

1. You will come to the University of Toronto for an interview about your sleep, your mood and your communication. You will also be asked to fill in some questionnaires about sleep, mood and communication. You will have a choice if you do not want to answer all the questions. We will also talk with someone who knows your sleep (if possible).These interviews and questionnaires will be done to assess your eligibility and the fact that depending on results, there is a chance that you will not be eligible to participate in the study. Should you decide to participate in this study, then you will be expected to complete all sections of the study.
2. The study involves 3 visits with one of the researchers; 1 for the initial interview, and 2 for the testing of your thinking and communication. The first visit will take about an hour and the second and third will take about two hours. During the second and third visits we will also talk with someone who knows your communication abilities. The second and third sessions will take place at Sunnybrook.
3. The study also involves an assessment of your sleep and an overnight sleep study at Sunnybrook Hospital, and a follow-up visit with the sleep doctor to see how you are responding to treatment. The treatment of your sleep will be the routine standard of care. We will try our best to co-ordinate the timing of the sleep tests with the assessment of your thinking and communication, to minimize the number of visits you need to make.
4. At the completion of the study, participants will be invited to a group feedback session (which will be held either at Sunnybrook Hospital or the University of

Toronto) to share the final results and findings with no identifying individual details. Attendance at this session is not mandatory, and is for those who are interested.

To compensate you for your time and travel expenses, you will be paid $120 upon completion for participating in this study.

What are the Risks of Participating in this Study? and Benefits

There are no known risks associated with any of the tasks that you will be asked to perform. Some tasks may seem very simple, while others will seem difficult. The more difficult tasks, including some of the neuropsychological tasks, may cause you to feel some stress.

What are the Benefits of Participating in this Study?

Participating in this study does not guarantee any immediate benefits to you directly, although you will be provided with an assessment and treatment of your sleep for the duration of the study, and an opportunity to learn how your sleep impacts your day-to-day function and recovery. However, the knowledge gained will contribute to the future treatment of other people with TBI. If new information pertaining to risks/benefits of the study is obtained, you will be notified.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The investigator(s) may decide to remove you from this study without your consent for if you are unable or unwilling to follow the study procedures.

If you are removed from this study, the investigator(s) will discuss the reasons with you and plans will be made for your continued care outside of the study.

You can also choose to end your participation at any time. If you withdraw voluntarily from the study, you are encouraged to contact Ms. Wiseman-Hakes at 416 946-8575. You may be asked questions about your experience with the study. You will be asked to continue your medical treatment and to cooperate in having whatever laboratory tests and examinations are considered necessary to safely look after your health. You can continue to receive medical care from Dr. Murray without participating in this research study, or can transfer your care to another physician if you wish.

WHAT ARE THE COSTS OF PARTICIPATING IN THIS STUDY?

Participating in this study may result in added costs to you for transportation, parking and lunch (or other meals),etc. Although you will not have to pay for any study medications you take while participating in this study, you may need to pay for medications to treat the side effects that you may experience as a result of participating in

this study. Your private health care insurer may not pay for all of these added costs. If you require treatment with continuous positive airway pressure as part of your routine care, the full cost may not be paid for by your medical insurance, but we will try and facilitate coverage where possible. This expense would be present whether or not you participate in the research study.

ARE STUDY PARTICIPANTS PAID TO PARTICIPATE IN THIS STUDY?

If you decide to participate in this study, you will be reimbursed $120 for some study related expenses such as parking, taxi, lunch. You will receive payment at the completion of the study, specifically, after you have completed the last (second) assessment of your thinking and communication abilities. If you decide to leave the study, you will receive a prorated payment for participating in the study. If you do not have insurance or other coverage, the costs of your treatment will be covered for the duration of the study. Should you decide to continue the treatment after the study is finished, you will be responsible for those ongoing costs.

WHAT OTHER CHOICES ARE THERE?

If you decide not to participate in this study, you can ask your family doctor for a referral for an assessment of your sleep, and a referral for an assessment by a speech language pathologist and neuropsychologist.

DO THE INVESTIGATORS HAVE ANY CONFLICTS OF INTEREST?

One of the investigators, Ms. Catherine Wiseman-Hakes is conducting this study in fulfillment of the requirements for the PhD (Doctor of Philosophy) in Rehabilitation Science, in the faculty of medicine at the University of Toronto. Ms Wiseman-Hakes is receiving a salary from the Canadian Institutes for Health Research (CIHR) to support her work on this study. Funding from this award will be used to pay for treatments where not otherwise covered, while you are participating in this study.

COMMUNICATION WITH YOUR FAMILY DOCTOR

For the purposes of this research study we will/are required to inform your family doctor of your participation in this study. The results of the sleep study and recommendations for treatment will be communicated to your family doctor and (if applicable) to the doctor who referred you to this study, as part of the routine standard of care.

Confidentiality

All information obtained during the study will be held in strict confidence. No names or identifying information (e.g., phone number) will be recorded on any response nor used in any publications or presentations. No identifying information will be used in any publication or presentation without your consent. All data will be kept in locked filing cabinets and/or password-protected computer files.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

All participants in a research study have the following rights:

1. You have the right to have this form and all information concerning this study explained to you and if you wish translated into your preferred language.

2. Participating in this study is your choice (voluntary). You have the right to refuse to participate, or to stop participating in this study at any time without having to provide a reason. If you choose to withdraw, it will not have any effect on your future medical treatment or health care. Should you choose to withdraw from the study you are encouraged to contact Ms. Wiseman-Hakes at 416 946-8575, immediately.

3. You have the right to receive all significant information that could help you make a decision about participating in this study. You also have the right to ask questions about this study and your rights as a research participant, and to have them answered to your satisfaction, before you make any decision. You also have the right to ask questions and to receive answers throughout this study. If you have any questions about this study you may contact the person in charge of this study Catherine Wiseman-Hakes at 416 946-8575. If you have questions about your rights as a research participant or any ethical issues related to this study that you wish to discuss with someone not directly involved with the study, you may call Daniel Gyewu, Research ethics coordinator at the University of Toronto, Faculty of Medicine at 416 946-3273.

4. By signing this consent form, you do not give up any of your legal rights.

5. You have the right to receive a copy of this signed and dated informed consent package before participating in this study.

6. You have the right to be told about any new information that might reasonably affect your willingness to continue to participate in this study as soon as the information becomes available to the study staff. This may include new information about the risks and benefits of being a participant in this study.

7. If you become sick or injured as a direct result of your participation in this study, your medical care will be provided.

8. Any of your personal information (information about you and your health that identifies you as an individual) collected or obtained, whether you choose to participate or not, will be kept confidential and protected to the fullest extent of the law. All personal information collected will be kept in a secure location. The study staff, the Sunnybrook Research Ethics Board, will have access to your personal

information for purposes associated with the study, but will only be allowed to access your records under the supervision of the Principal Investigator and will be obligated to protect your privacy and not disclose your personal information. None of your personal information will be given to anyone without your permission unless required by law. When the results of this study are published, your identity will not be disclosed. The data for this study will be retained for 10 years.

9. If, as a result of your participation in this study, any new clinically important medical information about your health is obtained, you will be given the opportunity to decide whether you wish to be made aware of that information.

10. You have the right to access, review and request changes to your personal information (i.e. address, date of birth).

11. You have the right to be informed of the results of this study once the entire study is complete.

DOCUMENTATION OF INFORMED CONSENT

Full Study Title: *Sleep Disorders Following Moderate- Severe Traumatic Brain Injury; Impact on Recovery of Cognitive-Communication Performance*

Name of Participant: _____

Participant
By signing this form, I confirm that:
- This research study has been fully explained to me and all of my questions answered to my satisfaction
- I understand the requirements of participating in this research study
- I have been informed of the risks and benefits, if any, of participating in this research study
- I have been informed of any alternatives to participating in this research study
- I have been informed of the rights of research participants
- I have read each page of this form
- I authorize access to my personal health information (medical record) and research study data as explained in this form
- I have agreed to participate in this study or agree to allow the person I am responsible for to participate in this study
- I understand that my family doctor will be informed of my participation in this research study
- This informed consent document will be placed in my medical records

_____	_____	_____
Name of participant (print)	Signature	Date

Person obtaining consent
By signing this form, I confirm that:
- I have explained this study and its purpose to the participant named above
- I have answered all questions asked by the participant
- I will give a copy of this signed and dated document to the participant

_____	_____	_____
Name of Person obtaining consent (print)	Signature	Date

Statement of Investigator
I acknowledge my responsibility for the care and well being of the above participant, to respect the rights and wishes of the participant as described in this informed consent document, and to conduct this study according to all applicable laws, regulations and guidelines relating to the ethical and legal conduct of research.

_____	_____	_____
Name of Investigator (print)	Signature	Date

ASSISTANCE DECLARATION ☐ (check here if not applicable)

The participant/substitute decision-maker was assisted during the consent process as follows:

- ❑ The consent form was read to the participant/substitute decision-maker, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant/substitute decision-maker.
- ❑ The person signing below acted as a translator for the participant/substitute decision-maker during the consent process. He/she attests that they have accurately translated the information for the participant/substitute decision-maker, and believe that that participant/substitute decision-maker has understood the information translated.

_____	_____	_____
Name of Person Assisting (Print)	Signature	Date

Appendix K

Telephone Script

Telephone Script

Hello, May I speak to _____

My name is Catherine Wiseman-Hakes and I am a researcher at the University of Toronto. I understand that you may be interested in learning more about our research study, "Sleep disorders following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance".

Let me tell you a bit about the study. We are interested in learning more about the relationship between sleep post injury, and the recovery of aspects of communication. Specifically, we want to learn about how sleep affects our/your ability to pay attention to things we hear such as conversation, your ability to follow quickly moving or complex conversations, and your ability to remember information. We also want to learn about how this may affect your functional day-to-day communication abilities. (Pause and ask if any questions, is there anything you would like me to explain again?)

Are you still interested? Do I have your permission to ask you some personal health history questions? Yes_____ No_____ *(Note if this information has already been provided by the referring clinician: see clinician referral form, then only those questions which still require answers will be asked).*

What is your date of birth ? _____
When did you have your brain injury? _____
How did you have your injury? _____ (to see if it is traumatic as opposed to acquired)
Did your doctors tell you if it was moderate or severe? (Or did they tell you it was mild?)
____
Do you know your Glasgow Coma Score (GCS) ? _____
After your injury were you in a coma? _____
If so, do you know for how long ? _____

Do you have difficulties sleeping since your injury? _____
Do you ever fall asleep in places outside of your bed when you don't want to, or have difficulty staying awake or functioning during the day?

Can you tell me about that?

_____
_____
_____
_____
_____

Have you seen a speech language pathologist since your injury? _____

Do you have difficulty paying attention or concentrating for periods of time? _____

Do you have any difficulty listening to and following conversations? _____ In any situations? _____ Please describe _____

Do you have any difficulty remembering things since your injury? _____

Can I tell you some more about what the study involves? _____

To participate in this study, you would first have an interview that takes about an hour in total, to learn more about your sleep, any sleep problems you may be having, and to learn more about how this is affecting you. We can schedule this interview at your convenience. If you share a bed with someone, we would like to ask them some questions about your sleep as well. Ideally we would like you to come to the University of Toronto for the interview, and we would cover your transportation costs such as parking or taxi. If this poses difficulty for you, we could arrange to do the interview over the phone, or possibly come to your home. (pause, ask if they have any question, or if there is anything they would like repeated or explained)

After the interview, if you are interested in continuing, and we feel that you fit our study, you would begin filling out a brief scale to monitor your sleep on a daily basis. We would speak to your family doctor to arrange for you to see a sleep physician (doctor) at either Sunnybrook Hospital or Toronto Western Hospital. You would also have an overnight sleep study in a sleep laboratory so we can see the exact problems you are having. (pause, ask if there is anything they would like repeated or explained).

At the same time, you would participate in some testing of your attention and your memory, and we would have you answer some questions about your communication in daily activities. We would also want to ask some questions to someone who sees you communicate in typical daily situations.

After you have the sleep study, the sleep physician will offer you some treatment for your sleep problem. The type of treatment will depend on the type of problem they find. Once you and the physician decide that the treatment is working, you will be asked to come back and repeat the tests of your attention, memory and communication. We will cover the costs of your treatment while you are in the study.

After you have finished the study, you will be given $120 dollars.

You have the right to withdraw from the study at any time.

Do you have any questions?

Are you interested in coming in for the first interview to see if you are a good fit for the study? _____

If so, I am going to send you a consent form which we will need you to sign when we meet. I will go through the consent form with you at that time and answer any questions you may have. I can also give you the consent form when we meet if that is what you would prefer. (mail ___ in person ____) I would also like to make an appointment for you to come in to have the initial interview. The times that are available are……

Do you need any help arranging transportation? ____

I will give you a reminder call the day before to remind you of your appointment.

Appointment scheduled for _____

Thank-you for your time.

Appendix L

Referral for Sleep Evaluation

Referral for Sleep Evaluation: As per discussion with Catherine Wiseman-Hakes

To: Brian James Murray, MD FRCP(C) D,ABSM
Neurology and Sleep Medicine
Sunnybrook Health Sciences Center M1-600
2075 Bayview Avenue
Toronto, Ontario, Canada, M4N 3M5
phone 416-480-6100 x2461
fax 416-480-6092

Date: _____ _____

Name of patient: _____ _____

OHIP #: _____ _____

DOB: ____ _____

Contact phone number: _____

Name of referring physician ___ _____

Address:

Phone:

Comments:

Evaluation and treatment of sleep and wakefulness and confounding factors post TBI.

Brief History:

_____

_____

Current Medications:

Appendix M

Letter of Participation to General Practitioner

Date _____

Dear Dr. _____

Your patient _____ has signed an informed consent to participate in a research study entitled "Sleep/wake disturbance following moderate-severe traumatic brain injury; Impact on recovery of cognitive-communication performance". Please see the attached letter for information regarding this study, and copy of signed consent.

Part of this study involves having an assessment of sleep including polysomnography to be conducted at Sunnybrook Health Sciences Centre. All participants will be seen by neurologist and sleep specialist Dr. Brian Murray, who will provide diagnosis and treatment for the sleep disturbance. As this component of the study is part of routine clinical care, a referral is required. We are requesting that you send a referral (via fax) for a sleep assessment to;

Brian James Murray, MD FRCP(C) D,ABSM
Neurology and Sleep Medicine
Assistant Professor, University of Toronto Sunnybrook Health Sciences Center M1-600
2075 Bayview Avenue
Toronto, Ontario, Canada, M4N 3M5
phone 416-480-6100 x2461
fax 416-480-6092

Please state that the referral is for the research study, as it will facilitate a timely referral. Should you have any questions, please do not hesitate to contact me directly.

Yours truly,

Catherine Wiseman-Hakes, M.Sc. Ph.D. (candidate)
Graduate Dept. of Rehabilitation Science,
Faculty of Medicine, University of Toronto
Study coordinator and principal investigator
416 946-8575

Appendix N

Harm Protocal List of Support Services

1. **Toronto Rehab Institute– Neurorehab Program Acquired Brain Injury Clinic**
   The Acquired Brain Injury Program (ABIP) serves the needs of adults with acquired brain injuries and their families.

   The program is based at 550 University Ave.

   Toronto, ON, M5G 2A2

   Phone: (416) 597-3422 ext. 3000 or 3593

2. **Toronto Community Care Access Centre**

   The community care access centres (CCACs) have a mandate to provide information about – and referral to – a wide range of community health and support services.

   Address: Central Toronto Community Office
   250 Dundas Street West

   Phone: (416) 506 -9888
   1-846-243-0061 (toll-free)

3. **Brain Injury Services of Toronto**

   Address: 660 Eglington Ave. E
   Box 4999
   Toronto, M4G 4G1

   www.bist.ca
   Email: info@bist.ca

4. **Ontario Brain Injury Association**
   Phone: 1-800-263-5404
   Web address: www.obia.on.ca

5. **Acquired Brain Injury Network Toronto**
   520 Sutherland Drive Toronto, Ontario M4G 3V9 Tel: 416-597-3057 Fax: 416-597-7021
   web address: http://www.abinetwork.ca/home.htm

   Has an application for services link on home page and can facilitate referrals

Appendix O

Permission to Reprint Letters

UTORmail :: Inbox: Re: Republication Permissions Request 12-04-17 10:08 PM

UNIVERSITY OF TORONTO

WELCOME TO UTORwebmail

MY.UTORONTO.CA ROSI FEEDBACK

Inbox

Inbox: Re: Republication Permissions Request (103 of 194)

Mark as: Move | Copy This message to Back to Inbox

Delete | Reply | Forward | Redirect | View Thread | Blocklist | Acceptlist | Message Source | Resume | Save as | Print

Date: Thu, 5 Apr 2012 11:36:06 -0400 [04/05/2012 11:36:06 AM EDT]
From: Permissions@guilford.com
To: Guilford Website User <catherinew.hakes@utoronto.ca>
Subject: Re: Republication Permissions Request
Part(s): Download All Attachments (in .zip file)
Headers: Show All Headers

Alternative parts for this section:
unnamed [text/html] 4.75 KB

Dear Catherine,

Thank you for your request.

Permission is hereby granted for the use requested at no charge. Please print out this email for your records as no other paperwork will be sent to you.

Any third party material is expressly excluded from this permission. If any of the material you wish to use appears within
our work with credit to another source, authorization from that source must be obtained.

This permission does not include the right for the publisher of the new work to grant others permission to photocopy or otherwise reproduce this material except for versions made by non-profit organizations for use by the blind or handicapped persons.

Credit line must include the following:
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Kind regards,

Tod Thilleman
Subsidiary Rights Associate

https://webmail.utoronto.ca/imp/message.php?index=5760 Page 1 of 3

Guilford Press
72 Spring Street
New York, NY 10012
(212) 431-9800
(212) 966-6708 fax
http://www.guilford.com

catherinew.hakes@utoronto.ca (Guilford Website User)
04/03/2012 12:02 PM

To
permissions@guilford.com, guilford2@formatease.com,
cc

Subject
Republication Permissions Request

Below is the result of your feedback form. It was submitted by
Guilford Website User (catherinew.hakes@utoronto.ca) on Tuesday, April 03,
2012 at 12:02:04
---

name: Catherine Wiseman-Hakes

inst: University of Toronto

add1: Graduate Department of Rehabilitation Science

add2: 16-500 University Ave

city: Toronto

state: Ontario

zip: M5G 1V7

country: Canada

phone: 416 946-8575

fax: 416 946-8570

GP_title: Insomnia: Psychological Assessment and Management

isbn: 1-57230-120-1

author: Charles M Morin

author_yesno: no

chapter: Appendices

figures: Appendices A and B

pagenum: 195-200

pubyear: 1993

yourtitle: Doctoral candidate, University of Toronto

yourtitle_auth: Catherine Wiseman-Hakes

publisher: not applicable

pubdate: August 2012

comments: I am completing a PhD thesis in the Graduate department of Rehabilitation Science at the University of Toronto, entitled 'Sleep and Wake disorders following traumatic brain injury: Impact on recovery of cognition and communication. These 2 appendices were used as data collection measures in my thesis and I am requesting permsision for them to be included in the appendix of the thesis. The thesis will be submitted to the national thesis program at Library and Archives Canada and will be made publicly available on the Theses Canda Portal. Thank-you for your consideration, Catherine Wiseman-Hakes

---

Date: Tue, 10 Apr 2012 08:40:26 -0500 [04/10/2012 09:40:26 AM EDT]
From: "HAS-SAT Shared Dist. and Licensing" <pas.Licensing@pearson.com>
To: catherinew.hakes@utoronto.ca
Subject: Permission Request related to including the BDI-II and BAI in a dissertation
Part(s): Download All Attachments (in .zip file)
Headers: Show All Headers

Alternative parts for this section:
unnamed [text/html] 10.90 KB

Dear Ms Wiseman-Hakes,

The Beck Depression Inventory-II (BDI-II) and the Beck Anxiety Inventory (BAI) are sensitive clinical assessments that require a high degree (B Level, Q1 or Q2) to purchase, administer, score and interpret. They also represent Pearson copyright and trade secret material. As such, Pearson does not permit photocopying or other reproduction of our test materials by any means and for any purpose. Please see the below guidance and restrictions on including the tests in dissertations.

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Consequently, your request is not approved.

Regards,

William H. Schryver
Senior Licensing Specialist
Clinical Assessment
Pearson
19500 Bulverde Road
San Antonio, TX 78259
T: (210) 339-5345
F: (210) 339-5059
E: pas.licensing@pearson.com

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From: catherinew.hakes@utoronto.ca [mailto:catherinew.hakes@utoronto.ca]
Sent: Mon 4/9/2012 7:09 PM
To: HAS-SAT Shared Dist. and Licensing; HAIWEBADMIN (HAS-SAT)
Subject: Permission Requests

The following is feedback submitted via the Contact Us page on the www.PearsonAssessments.com Website:

Contact Information	
Name:	Ms Catherine A Wiseman-Hakes
Position / Title:	PhD student
Company Name:	University of Toronto
Email Address:	catherinew.hakes@utoronto.ca
Address:	Graduate Dept of Rehabilitation Science University of Toronto 160-500 University Ave
City, State, Zip:	Toronto, Other, M5G 1V7
Country/Region:	CA
Telephone:	416 946-8575 (or cell 416 451 7167)
Fax:	416 946-8570

Legal Department/Permission Requests	
Title of publication:	Beck Depression and Anxiety Inventories
Edition:	1993
Author, if available:	Aaron T Beck
Copyright Date:	1990, 1987

Brief description of your request: I am completing a Doctor of Philosophy degree in the Graduate Department of Rehabilitation Science, at the University of Toronto. My thesis is entitled "Sleep/wake Disorders Following Traumatic Brain Injury; Impact on Recovery of Cognition and Communication". I have used the Beck Depression and Anxiety Inventories as two of the outcome measures for this study.

I am writing to request permission to include the questionnaires from the Beck Depression

and the Beck Anxiety Inventories in the appendix of the thesis, and permission for the Library and Archives Canada to make use of the thesis i.e. reproduce, publish, archive, preserve, conserve, communicate to the public by telecommunication or on the Internet, loan, distribute and sell my thesis (the title of which is set forth above) worldwide, for commercial or non-commercial purposes, in microform, paper, electronic and/or any other formats.

Thank-you for your consideration!

Specific list of materials to reproduce: Beck Depression Inventory Beck Anxiety Inventory (note: test forms only)

Number of subjects/copies needed per year: 0
Name of responsible party: Catherine Wiseman-Hakes
Inclusive Dates: 2012

Adaptation and/or format changes required: scannable format

Is this request for permission to translate? No
Is this request for permission to use materials in a book? No

Catherine Wiseman-Hakes
Graduate Dept. of Rehabilitation Science
University of Toronto, 160-500 University Ave
Toronto, Ontario, Canada
M5G 1V7

April 3, 2012

Dr Jacinta Douglas, Associate Professor
Dept of Human Communication Sciences
La Trobe University
HS1-334 Melbourne (Bundoora)
j.douglas@latrobe.edu

Dear Jacinta,

As you may recall, I am completing a doctoral thesis in the Graduate Department of Rehabilitation Science at the University of Toronto, entitled 'Sleep and wake disorders following traumatic brain injury: Impact on recovery of cognition and communication.' As required, the thesis will be will be submitted to the national thesis program at Library and Archives Canada and will be made publicly available on the Theses Canada Portal. As you may also recall, I have used the La Trobe Communication Questionnaire as one of my outcome measures. I am writing to request permission to include the Latrobe QC in the thesis appendix and for the Library and Archives Canada to reproduce, publish, archive, preserve, conserve, communicate to the public by telecommunication or on the Internet, loan, distribute and sell the thesis worldwide, for commercial or non-commercial purposes, in microform, paper, electronic and/or any other formats. The material to be reprinted is the Latrobe Communication Questionnaire. You will be acknowledged as the author and source.

CQ (TD)

If these arrangements meet with your approval, please sign this letter below where indicated and return to me by email or fax 416 946-8570. I thank you in advance for your cooperation and understanding.

Sincerely,

Catherine Wiseman-Hakes

PERMISSION GRANTED FOR THE USE REQUESTED ABOVE

[signature]	DR JACINTA DOUGLAS	18 April 2012
Signature	Print Name and Title	Date

Appendix P

Insomnia Severity Index

Insomnia Severity Index (ISI)

ID#: _____ **Date: _____**

1. Please rate the current (i.e., last 2 weeks) **SEVERITY** of your insomnia problem(s).

	None	Mild	Mod	Severe	Very Severe
Difficulty falling asleep:	0	1	2	3	4
Difficulty staying asleep:	0	1	2	3	4
Problem waking up too early:	0	1	2	3	4

2. How **SATISFIED**/dissatisfied are you with your current sleep pattern?

Very Satisfied				Very Dissatisfied
0	1	2	3	4

3. To what extent do you consider your sleep problem to **INTERFERE** with your daily functioning (e.g. daytime fatigue, ability to function at work/daily chores, concentration, memory, mood, etc.).

Not at all	A Little	Somewhat	Much	Very Much
0	1	2	3	4

4. How **NOTICEABLE** to others do you think your sleeping problem is in terms of impairing the quality of your life?

Not at all Not Noticeable	Barely	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

5. How **WORRIED/**distressed are you about your current sleep problem?

Not at all	A Little	Somewhat	Much	Very Much
0	1	2	3	4

Guidelines for Scoring/Interpretation:

Add scores for all seven items (1a+1b+1c+ 2+3+4+5) = ____
Total score ranges from 0-28
0-7 = No clinically significant insomnia
8-14 = Subthreshold insomnia
15-21 = Clinical insomnia (moderate severity)
21-28 = Clinical insomnia (severe)

Appendix Q

Diagnostic Interview for Insomnia

Diagnostic Interview for Insomnia:

Demographic Information:
ID#_____ **Occupation** _____

Gender _____ **Education** _____

Age_____ **Marital Status**_____

1. Nature of Sleep Wake Problem

Do you have a problem with falling asleep?	No	Mild	Moderate	Severe
Do you have a problem staying asleep?	No	Mild	Moderate	Severe
Do you have a problem with waking up too early in the morning?	No	Mild	Moderate	Severe
Do you have a problem staying awake during the day?	No	Mild	Moderate	Severe

2. Current Sleep-wake Schedule

What is your usual bedtime on weekdays?	_____ o'clock
At what time do you last awaken in the morning?	_____ o'clock
What is your usual arising time in the morning?	_____ o'clock
Do you have the same sleep-wake schedule on weekends?	Yes _____ No_____
How often do you take naps? (Including unintentional naps)	_____ Days/week
Do you ever fall asleep at inappropriate times or places?	Yes _____ No_____
How many nights/week do you have a problem with falling/staying asleep?	_____ Nights
On a typical night (past month), how long does it take you to fall asleep after you go to bed and turn the lights off?	____hours ____ minutes
On a typical night (past month), how many times do you wake up during the middle of the night?	_____ Times
What wakes you up at night? (circle any that apply) Pain, noise, nocturia, child, partner, spontaneous	
On a typical night, how long do you spend awake in the middle of the night? (Total # of minutes/hours for all awakenings)	____hours ____ minutes
How many hours of sleep per night do you usually get?	____hours ____ minutes

3. Sleeping Aids

In the past 4 weeks have you used sleeping pills? Yes _____ No_____

Which drugs? Prescribed, over the counter or both? _____

_____

What dosage? _____

How many nights per week? _____

If no, have you ever? _____

When did you first use sleep medication? _____

When did you last use sleep medication? _____

In the last 4 weeks, have you used alcohol as a sleep aid? Yes _____ No_____

What kind and how many ounces? _____

How many nights per week? _____

If no, have you ever? _____

4. Sleep Problem History (Onset, course, duration)

How long have you been suffering from insomnia? Years_____ Months _____

Were there any stressful life events related to its onset? (example; death of a loved one, divorce,, retirement, Medical or emotional problem?) _____

Gradual or sudden onset? (circle)

What has been the course of your Insomnia problem since Its onset (persistent, episodic, seasonal etc.) _____

5. Bedroom Environment

Are you sleeping with a bed partner (including pet) Yes _____ No_____

Is your mattress comfortable? Yes _____ No_____

Is your bedroom quiet? Yes _____ No_____

Do you have a TV, radio, digital clock, computer or Phone in your bedroom Yes _____ No_____

Is there a desk with paperwork to be done in the bedroom? Yes _____ No_____

Do you read in bed before bedtime? Yes _____ No_____

What is the temperature in your room at night? _____

6. Eating, Exercise and Substance Use Habits

How many times per week do you exercise? _____

Do you sometimes exercise prior to bedtime? Yes _____ No_____

How many caffeinated beverages do you drink per day? _____

After dinner?

How many cigarettes per day do you smoke per day? _____

How many ounces of alcohol per day do you drink? _____

Liquid intake in the evening? _____

7. Functional Analysis

What is your pre bedtime routine like?

What do you do when you can't fall asleep or return to sleep?

Is your sleep better/worse/same when you go away from home?

Is your sleep better/worse/same on weekends?

What types of factors exacerbate your sleep problem (e.g. stress at work, travel plan etc.)

What types of factors improve your sleep? (e.g. vacation, sex etc.)

How concerned are you about sleep/insomnia?

What impact does insomnia have on your life? (mood, alertness, performance)

How do you cope with these day time sequelae?

Have you received treatment in the past other than sleeping aids?

What prompted you to seek insomnia treatment at this time?

8. Symptoms of Other Sleep Disorders

Have you or your spouse ever noticed one of the following, and if so, how often on a typical week would you say you experience these symptoms?

A. *Restless legs*: Crawling or aching feeling in the legs (calves) and inability to keep legs still.
B. *Periodic limb movements*: Leg twitches or jerks during the night; waking up with cramps in legs.
C. *Apnea*: Snoring, pauses in breathing at night, shortness of breath, choking at night, morning headaches, chest pain, dry mouth.
D. *Narcolepsy*: Sleep attacks, sleep paralysis, hypnagogic hallucinations, cataplexy.
E. *Gastro-esophageal reflux*: Sour taste in mouth, heartburn, reflux.
F. *Parasomnias*: Nightmares, night terrors, sleepwalking/talking, bruxism.
G. *Sleep-wake schedule disorder*: Rotating shift, or night shift work.

Diagnostic Impressions

9. Medical History/Medication Use

Last physical exam: Weight _____ Height _____

Current medical problems:

Current medications:

Hospitalizations/surgery:

10. History of Psychopathology/Psychiatric Treatment (adapted from the DSM-III-R (SCID))

Are you currently psychological or psychiatric treatment for emotional or mental health problems?		Yes _____ No_____		
Have you or anyone in your family ever been treated for Emotional or mental health issues in the past?		Yes _____ No_____		
Have you or anyone in your family ever been a patient in a psychiatric hospital?		Yes _____ No_____		
Has alcohol or any drug ever caused a problem for you?		Yes _____ No_____		
Have you ever been treated for any alcohol/substance abuse problems?		Yes _____ No_____		
Has anything happened lately that has been especially hard for you?		Yes _____ No_____		
What about difficulties with your work or family?		Yes _____ No_____		
In the last month, has there been a period of time when you were feeling depressed or down most of the day, nearly every day? If yes, as long as 2 weeks?	?	1	2	3
What about being a lot less interested in most things or being Unable to enjoy the things you used to enjoy? If yes, was it nearly every day?	?	1	2	3
For the past couple of years, have you been bothered by depressed mood most of the day, more days than not? more than half the time?	?	1	2	3
Have you ever had a panic attack, when you suddenly felt anxious, frightened or extremely uncomfortable? If yes, 4 attacks within 1 month?	?	1	2	3
Have you ever been afraid of going out of the house alone, Being in crowds, standing in a line, or travelling on buses, subways or trains?	?	1	2	3
Have you ever been bothered by thoughts that didn't make any sense and kept coming back to you even when you tried not to have them?	?	1	2	3
In the last 6 months, have you been particularly nervous or anxious?	?	1	2	3
Do you worry a lot about terrible things that may happen?	?	1	2	3
During the last 6 months, would you say that you have been worrying most of the time (more days than not?)	?	1	2	3

If psychopathology is present, evaluate its onset and temporal course in relation to the sleep disturbance.

Does insomnia occur exclusively during the course of anxiety/depression episodes? Yes_____ No_____

Diagnostic Impression: ? = inadequate information, 1 = Absent or false, 2 = Sub threshold 3 = Present

Appendix R

Latrobe Communication Questionnaire

LA TROBE COMMUNICATION QUESTIONNAIRE

by Jacinta Douglas, Christine Bracy & Pamela Snow

LCQ-Close Other Form: Frequency

Name or ID #:_____ Age:_____ Gender: M F Date:____/_____/____

Patient Name/ID#:_____ Relationship to patient:_____

Instructions: The following questions ask about aspects of _____ communication. For **every** question please circle the response which best answers the question, where:

1 = Never or Rarely 2 = Sometimes 3 = Often 4 = Usually or Always

Make sure you consider ***all*** the communication situations encountered in daily life (e.g. family, social and work situations).

WHEN TALKING TO OTHERS DOES _____:		**FREQUENCY**				
1.	**Leave out important details?**	**1**	**2**	**3**	**4**	
2.	Use a lot of vague or empty words such as "you know what I mean" instead of the right word?	**1**	**2**	**3**	**4**	
3.	**Go over and over the same ground in conversation?**	**1**	**2**	**3**	**4**	

4.	Switch to a different topic of conversation too quickly?	**1**	**2**	**3**	**4**	
5.	**Need a long time to think before answering the other person?**	**1**	**2**	**3**	**4**	
6.	Find it hard to look at the other speaker?	**1**	**2**	**3**	**4**	
7.	**Have difficulty thinking of the particular word he/she wants?**	**1**	**2**	**3**	**4**	
8.	Speak too slowly?	**1**	**2**	**3**	**4**	
9.	**Say or do things others might consider rude or embarrassing?**	**1**	**2**	**3**	**4**	
10.	Hesitate, pause and/or repeat him/herself?	**1**	**2**	**3**	**4**	
11.	***Know when to talk and when to listen?***	***4***	***3***	***2***	***1***	
12.	Get side-tracked by irrelevant parts of conversations?	**1**	**2**	**3**	**4**	
13.	**Find it difficult to follow group conversations?**	**1**	**2**	**3**	**4**	
14.	Need the other person to repeat what they have said before being able to answer?	**1**	**2**	**3**	**4**	
15.	**Give people information that is not correct?**	**1**	**2**	**3**	**4**	

FREQUENCY: 1 = Never or Rarely 2 = Sometimes 3 = Often 4 = Usually or Always

WHEN TALKING TO OTHERS DOES _____:		**FREQUENCY**				
16.	Make a few false starts before getting his/her message across?	**1**	**2**	**3**	**4**	
17.	**Have trouble using his/her tone of voice to get the message across?**	**1**	**2**	**3**	**4**	
18.	Have difficulty getting conversations started?	**1**	**2**	**3**	**4**	
19.	***Keep track of the main details of conversations?***	***4***	***3***	***2***	***1***	
20.	Give answers that are not connected to the questions asked?	**1**	**2**	**3**	**4**	
21.	***Find it easy to change his/her speech style (e.g. tone of voice, choice of words) according to the situation he/she is in?***	***4***	***3***	***2***	***1***	
22.	Speak too quickly?	**1**	**2**	**3**	**4**	
23.	***Put ideas together in a logical way?***	***4***	***3***	***2***	***1***	
24.	Allow people to assume the wrong impressions from his/her conversations?	**1**	**2**	**3**	**4**	
25.	**Carry on talking about things for too long in his/her conversations?**	**1**	**2**	**3**	**4**	
26.	Have difficulty thinking of things to say to keep conversations going?	**1**	**2**	**3**	**4**	
27.	**Answer without taking time to think about what the other person has said?**	**1**	**2**	**3**	**4**	
28.	*Give information that is completely accurate?*	***4***	***3***	***2***	***1***	
29.	**Lose track of conversations in noisy places?**	**1**	**2**	**3**	**4**	
30.	Have difficulty bringing conversations to a close?	**1**	**2**	**3**	**4**	

Comments: If you have any additional comments to make, please do so in the space provided below.

Appendix S

Daily Cognitive-Communication and Sleep Profile (DCCASP)

Background: The Daily Cognitive-Communication and Sleep Profile (DCCASP) is a series of seven 5 point Likert rating scales developed for use in clinical practice and as a research tool, as a means of monitoring daily fluctuations in cognitive-communication function in relation to quality of sleep. As sleep is a dynamic process, a daily profile was found to be sensitive to subtle changes in sleep and function, and useful in identifying patterns and trends. The questionnaire is completed either by the client, therapist or significant other who has the opportunity to observe the client over the course of the day. Specifically, clients are asked to rate their functional performance in the domains of sustained attention/vigilance/executive attention to spoken or written communication, verbal memory (retention of spoken or written information), speed of language processing, and new learning of verbally mediated information, in addition to their sleep quality, level of fatigue, daytime sleepiness and mood. The profile has been found to be clinically and statistically sensitive to changes in cognitive-communication function (specifically, sustained auditory attention, language processing and verbal memory) in relation to changes in sleep quality. Results can be used to educate the client regarding the impact of their sleep patterns on daily cognitive-communication function, and can also be used to track subjective response to treatment of sleep and wake disturbances or changes in sleep and wake patterns.

Purpose:

The purpose of this log is to observe and document some of your cognitive-communication abilities over time and to see how they might be affected by the quality of your sleep. We want to see how you can ***pay attention and concentrate*** over time, how you can ***listen and follow conversations***, and how you can ***remember things that you have done or talked about*** during the day. We also want to look at your ***level of fatigue*** during the day, i.e. ***how tired you felt***, and if you ***wanted or needed to go to sleep during the day***. We also want to learn about your ***mood***. As our sleep may change on a daily basis, we want to see if any patterns emerge.

Instructions:

When should I fill out this log?

1. Ideally the log should be filled out on a daily basis because this will give us the best information to help learn about your sleep and day-time function. For some people it may help to fill it twice a day, as they may function differently in the morning and afternoon. If you forget to fill it out on any day, don't worry, just complete as much as you can.

What is in this log?

2. There are 7 sections to this log. These include; a) your quality of sleep the night last night, b) how tired you were during the day, c) how sleepy you felt and if you fell asleep during the day, d) whether or not you how you were able to pay attention and concentrate during the day, e) how you were able to listen and follow conversations or read during the day, f) how you were able to remember things during the day g) how was your mood during the day.

How do I rate the scales or decide on my scores for the day?

3. Each section has a scale from 1-5. **For all scales, 1 is the poorest score and 5 is the best score.** Before you begin, think about what a 5 might be like (i.e. a really good day) or a 1 might be like (i.e. a really bad day) for each section. For example, for "paying attention" maybe the number 5 means you could concentrate and do all the things you needed to do that day without loosing your focus. Maybe the number 1 meant that you couldn't concentrate on anything at all. Since everyone functions differently, we suggest that before you start filling out the log for the first time, you write down a description of what you think represents your number 5 (your best) and your number 1 (your worst) for each section so you can use that to compare how you felt today. Alternatively, you may also use the descriptions provided with the numbers as a guide.

   Decide which number best describes how you felt and how you were able to function for that specific day. Under each section there is a table with the days of the week, write that number in the box.

What if something different or important happened that day that affected my sleep or my day-time function?

4. On the last page of the D-CCASP, there is a section for you to write a comment(s) if you think it is helpful. Maybe something happened that day or week that you were worried about, or felt good about, or maybe you started a new medication or treatment. You can briefly write down anything that you think is important. If something happened on a specific day, please write down the day and date it occurred.

What if I have questions about how to fill this out?

5. Ideally your therapist will have explained the different terms to you. If you have any questions or you are not sure about what each of the terms mean, you can ask your therapist to go over them with you! They are there to help. If you are part of the research study, you can contact Catherine Wiseman-Hakes at 416 946-8575 or by email catherinew.hakes@uotoronto.ca

6. For clinicans; There is no composite score.

DCCASP: Write the number (from 1 – 5) that best describes how you felt today in the table below each section.

1. SQ How was your sleep quality for last night?

1 2 3 4 5

Worst Possible Sleep — Best Possible Sleep

DT Date	SUN	MON	TUE	WED	THU	FRI	SAT
SLEEP RATING							

SQ: Total for week___

Average_____

2. MD How was your mood for today?

1 2 3 4 5

Overall anxious, irritable, unhappy, restless, and easily annoyed, overwhelmed by my day.

Overall calm, reasonably content, able to handle what the day threw at me.

DT Date	SUN	MON	TUE	WED	THU	FRI	SAT
MOOD RATING							

MD: Total for week___

Average_____

3. FTG How tired did you feel today?

1	2	3	4	5
I felt really tired, low energy, unable to do my daily tasks				Good level of energy, able to do daily tasks with minimal difficulty.

DT Date	SUN	MON	TUE	WED	THU	FRI	SAT
FATIGUE RATING							

FTG: Total for week___

Average_____

4. NPS Did you fall asleep during the day today?

1	2	3	4	5
I fell asleep even though I didn't want to. I may not have been in my bed, but couldn't keep my eyes open.	I felt sleepy and fell asleep even though I didn't do anything too tiring	I felt sleepy and had to lie down and rest during the day after activities.	I felt sleepy but was able to stay awake.	I did not feel sleepy and was able to stay awake all day.

DT Date	SUN	MON	TUE	WED	THU	FRI	SAT
NAP RATING							

FTG: Total for week___

Average_____

5. ATTN Rate your attentiveness and concentration for today.

1	2	3	4	5
I couldn't concentrate today (following a conversation, reading, or watching a television program), and I couldn't block out things that distracted me, (eg. Pain, thoughts, ringing in the ears, background noises, conversations)	Really hard to pay attention. I kept focused briefly but got distracted.	Hard to pay attention but I can follow tasks and get back on track if distracted. May need help to get refocused.	Some difficulty paying attention and following tasks. I occasionally have to get back on track if distracted.	Fairly easy to block out distractions, I can pay attention for extended periods of time (eg. long enough to complete my daily tasks).

DT Date	SUN	MON	TUE	WED	THU	FRI	SAT
ATTN RATING							

ATTN: Total for week___

Average_____

6. MEM Rate your memory abilities for today.

1	2	3	4	5
Can't remember activities, events, or conversations from today.	If reminded, can remember the gist of some activities, events, or conversations from today.	With no reminders can remember the gist of some activities, events or conversations from today.	Can remember several details of activities, events or conversations from today.	Can remember almost all the details of activities, events or conversations from today.

DT Date	SUN	MON	TUE	WED	THU	FRI	SAT
MEM RATING							

MEM: Total for week___

Average_____

7. LP Rate your communication and conversation abilities for today.

1	2	3	4	5
I was unable to carry on a conversation today. My Conversation partner must always speak slower and simplify the topic.	I could carry on a conversation with one person, but need extra time to think and respond. At times conversation partner must speak slower and simplify the topic.	Can carry on a conversation with one person, helps when my conversation partner speaks slower. Can carry on multi-speaker conversations briefly if topic stays the same, but I need extra time to think and respond.	Can carry on a conversation with one person, conversation partner doesn't need to speak slower. Some difficulty following and responding to multi-speaker conversations, but I can do it.	Can keep up with and reply to a multi person or single person conversation with minimal difficulty.

DT Date	SUN	MON	TUE	WED	THU	FRI	SAT
LP RATING							

LP: Total for week___

Average_____

8. COMMENTS Did anything unusual or important happen that you think might have affected your sleep or day-time function?

_____

_____

_____

_____

_____

_____

_____

Appendix T

Medical Chart Sleep Findings:

Abstraction Form

Catherine Wiseman-Hakes: August 2011

Date of Sleep Study: _____Date of MWT (or MSLT): ____Date of data extraction:_____
Extraction done by: CWH

ID #	**Sex:**	**Time post injury**:	**BMI:**	**GCS:**	**TBI Dx / Severity**

Medications at time of study:

Co-morbidities:
Sleep diagnosis:

Sleep onset latency:	**Sleep duration:**	**Sleep efficiency:**
# of awakenings:	**REM latency:**	**RDI Index overall**:
RDI index NREM:	**RDI index REM:**	**# of arousals & arousal index**
PLM's:	**Lowest O2 Sat:**	**Staging:**

Comments:

Date of follow-up to review study:

Prescription

Appendix U

List of Abbreviations

Abbreviations	
TBI mTBI sTBI	Traumatic Brain Injury Mild traumatic brain injury Severe traumatic brain injury
HIV	Human immunodeficiency virus
AIDS	Acquired immune deficiency syndrome
DSM	Diagnostic and Statistical Manual of Mental Disorders
CCDs	Cognitive-communication Disorders
REM	Rapid eye movement
NREM	Non rapid eye-movement
EEG	Electroencephalography
EOG	Electro-oculography
EMG	Electromyography
SWS	Slow-wave sleep
SCN	Suprachisamatic nucleus
MWT	Multiple Wake test
ADL	Activities of daily living
PTSD	Post-traumatic stress disorder
ISI	Insomnia Severity Index
BDI	Beck Depression Inventory
BAI	Beck Anxiety Inventory
PSG	Polysomnography
MWT	Multiple Wake Test
MSLT	Multiple Sleep Latency Test
ICF	International Classification of Functioning, Disability and Health
WHO	World Health Organization