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Influence of nighttime interruptions on sleep and function of patients following traumatic brain
injury

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Abstract

Influence of Nighttime Interruptions on Sleep and Function of Patients following Traumatic
Brain Injury (TBI)

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In the United States, nearly 282,000 people are hospitalized for traumatic brain injury (TBI) each year. TBI includes patients with moderate and severe TBI. As a part of the clinical care continuum, intermediate care is traditionally the last stage of inpatient hospitalization for people with TBI cases in U.S. facilities. There, an interdisciplinary team evaluates a patient's recovery from brain injury to identify appropriate care referral which is usually a skilled nursing facility, inpatient rehabilitation, or home.

Unfortunately, while hospitalized the patient with TBI may encounter a care environment that is not always supportive of recovery. The environment of care is often a barrier and a facilitator to post-TBI recovery, because it influences important physiologic processes, notably sleep. It is a barrier because when there are excessive stimuli there is less rest. It is a facilitator because when these stimuli are curbed, there is a therapeutic effect that takes place. Overall, the

goal in the intermediate care environment is to minimize barriers and augment facilitators of health improvement.

In patients with TBI, both factors of intrinsic and extrinsic origin contribute to sleep disturbance and act as barriers. Among hospitalized patients of all kinds, extrinsic factors like hospital noise, exposure to light, and nighttime awakenings (either caused by hospital staff or occurring naturally in the patients themselves) are noted as salient barriers. These same problems can be assumed to also burden hospitalized patients with TBI. However the available literature on sleep disturbance of patients with TBI housed on intermediate care units is sparse. Current methods to describe the influence of the care environment on the sleep health of this patient population are also sparse. This may be due in part to the short and unpredictable length of stay for these patients when they are housed in intermediate care units—a phase of hospitalization where they are monitored until they are medically stable enough to be transferred to another level of care. Another challenge relates to conducting clinical research on a vulnerable population because it which requires more resources to obtain informed consent (support from legally authorized representative [LAR]). There is also the challenge of assessing sleep variables among a population with accompanying injuries and co-morbidities. Even if a retrospective study is implemented, there is the challenge of securing pertinent and consistent sleep and environmental information from the electronic medical record (EMR). More importantly, the challenge of not knowing the pattern of environmental and sleep characteristics of this group can prevent a nurse researcher from knowing what type of environmental curbing to focus on. For these reasons, the dual approach of documenting both sleep actigraphy and continuous external stimuli in the patient's room may be necessary for the development of pertinent care interventions.

The dissertation is composed of three manuscripts. The first manuscript aims to describe the utility of the EMR in identifying sleep health in patients with moderate-to-severe TBI who are housed in the neuroscience intermediate care setting. The second manuscript focuses on the methods for describing objective rest/activity characteristics during nighttime hours (using actigraphy) for hospitalized patients with moderate-to-severe TBI. The third manuscript describes the utility of continuously logging select external stimuli in the hospital rooms of patients being treated for a moderate-to-severe TBI.

The first manuscript is a retrospective chart review that describes documented nursing interventions and sleep health of patients with moderate-to-severe TBI (N= 34) housed in a neuroscience specialty unit of a level 1 trauma center during nighttime hours (2200 through 0800 hours). Subjects were identified from the trauma registry between January and March 2013. Data were extracted from both the trauma registry and the EMR. The variables of “mean nighttime care activities” and “slept well” were created based on nursing flow sheet logs and hospital notes during the nighttime hours for these patients for up to seven days. The results of the study show that while nightly nursing care activities are frequent (M = 5.6 activities per night), sleep/rest was poorly captured in nursing documentation. The paper highlights the absence of standard sleep/rest queries for nursing documentation in the EMR.

The second manuscript recounts actigraphy findings from a single-cohort feasibility study (N = 17) and specifically details the sleep parameters of patients with moderate or severe TBI who are hospitalized on a neuroscience specialty floor of a level 1 trauma center. This manuscript also discusses some of the challenges of conducting actigraphy on this population as well as the underlying methodology and data analysis scheme. Wrist actigraphy data were collected on subjects for five consecutive days or until discharge from the unit; only nighttime

sleep was analyzed. Injury and disability variables like Glasgow coma scale (GCS) and functional independence measure (FIM®), respectively, were also collected. Results from this study show that more than half the sample has sleep efficiencies of less than 80%. During the hours of sleep, the average number of wake bouts across the sample is frequent (M = 41 per person) and total wake time during the nighttime hours is excessive (M = 74 minutes), suggesting poor sleep consolidation in this group. Likely due to the small sample size, weak associations were found between the sleep parameters and primary injury/disability variables.

The third manuscript recounts findings from a single-cohort feasibility study (N = 18) that sought to describe the pattern of ambient environmental influences on the sleep of a patient with moderate or severe TBI during the nighttime hours of hospitalization on an intermediate care neuroscience specialty unit (2000 to 0800 hours). For up to five days or until discharge from the unit, wrist actigraphy and a custom, multi-sensor device continuously logged sleep-wake cycles and ambient stimuli, respectively, of a patient housed on the unit. The manuscript results show that sound and motion signaling significantly influences the probability of nighttime awakenings for patients in the sample. During nighttime hours, mean sound levels were 52 decibels (A-weighted); mean light levels were 9 lumens, and the mean proportion of movement was 0.28 (p) (28%). With the ambient stimuli set at their mean levels, there is a 20% probability that patients will wake during the night (multi-level logistic regression). The comprehensive results from these papers suggest that implementation of known (actigraphy) and novel (multi-sensor) technologies among this patient population could yield critical information about the pattern of sleep and the pattern of environmental stimuli.

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DEDICATION

I dedicate this dissertation to:

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My siblings Arnold, Shannel, Na'Tashia, Toni, Anthony, Jhaphia, & Joel

My entire family, both by blood and by selection

My church family and faith community in Orlando, FL and Seattle, WA

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Antwan a.k.a "Patient Zero"

Nursing staff on every neuroscience specialty floor

And several of my elementary, middle, and high-school teachers and administrators who

believed in me, fueled my ideas, and kept me on the right path.

*" But Jesus beheld them, and said unto them, **With men this is impossible; but with God all things are possible .**" Matthew 19:26*

CHAPTER 1: INTRODUCTION

Significance of the Problem

According to the most recent epidemiologic reports, 2.8 million adults in the United States suffered a traumatic brain injury (TBI) in 2013. Of these people, 282,000 required hospitalization (Taylor, Bell, Breiding, & Xu, 2017). TBI contributes to about a third (30%) of all disability in the United States; following a severe TBI, 43% of victims experience severe life-long disability and dependence on others (Selassie et al., 2008; Johnston, Shawaryn, Malec, Kreutzer & Hammond., 2006; Nalder et al., 2012; Rogers & Read, 2007). Brain injury can lead to both short-term and long-term disabilities, but the latter is a major cause for concern because sustained effects of brain injury can impair cognition, emotions, sensation, and motor functioning. Hospitalization for TBI accounts for almost 90% of the total cost of treatment of TBI in the US, and the estimated cost of treatment for TBI are upwards of \$76.5 billion (Finkelstein, Corso, & Miller, 2006). Due to both human and monetary costs, TBI remains a significant public health concern.

Classification of Traumatic Brain Injury Severity

There is no gold standard that categorizes the severity of a TBI, but there are several schools of thought on *how* TBI severity should be classified (Schwab, Gudmundsson, & Lew, 2015). The author classifies a moderate and severe TBI according to the following criteria: Glasgow Coma Scale score (GCS) between 3 and 11 (Jenett & Teasdale, 1977), a positive loss of consciousness, or neurological imaging that shows evidence of trauma-induced, intracranial, and extracranial abnormality.

The Multifactorial Nature of Sleep Disturbance in the Hospitalized Patient with TBI

The monitoring and surveillance of patients that occurs during hospitalization can create a care environment that does not always support recovery (Inouye, 2013). The care environment that will be the focus of this dissertation is that of the neuroscience intermediate-care unit—the phase of hospitalization which follows the intensive care unit (ICU) (Keenan & Joseph, 2010).

While housed in the intermediate-care unit, patients may experience clinical sleep complications resulting from their injuries and from the care environment itself (McNett, Sarver, & Wilczewski, 2012). The fact that hospitalized patients with TBI are vulnerable to clinical sleep complications that result from both their injuries *and* their physical environment of care exemplifies the multi-factorial nature of their sleep complications (Friese, 2008; Yoder, Yuen, Churpek, Arora, & Edelson, 2013). The sleep complication that will be the focus of this dissertation is nighttime awakenings.

A nighttime awakening is defined as an event where the subject—and, on occasion, the observer—readily perceive a change from a sleeping state to an activity state. Nighttime awakenings are a particularly important concept to study in hospitalized patients with moderate and severe TBI for two main reasons:

- Patients with moderate and severe TBI are predisposed to fragmented sleep—a class of sleep deprivation that manifests as the patient spontaneously waking from their sleep or from the patient’s inability to maintain restful sleep
- A hospitalized patient waking from sleep is likely to be the result of an interruption, usually one originating in the patient’s physical environment

I have just described the multifactorial nature of nighttime awakenings, a clinical sleep complication, in hospitalized patients with moderate and severe TBI. I will now explain how nighttime awakenings in patients with moderate and severe TBI are intrinsic and extrinsic in

origin (Friese, 2008; Watson, Dikmen, Machamer, Doherty, & Temkin, 2007; Yoder et al., 2013).

By *intrinsic*, I mean to cite the internal factors of nighttime awakenings in patients with TBI. These internal factors result from damage to brain circuitry that is responsible for regulating sleep and wakefulness (Viola-Saltman & Watson, 2012) and to situations that do not allow for rest (e.g. depression, anxiety) (Parcell, Ponsford, Rajaratnam, & Redman, 2006; Ponsford et al., 2012). These internal factors are, respectively, neuro-physiologic and neuro-psychological in origin. Conversely, *extrinsic* factors of nighttime awakenings in patients with TBI are external. They result from disruptions in the patient's physical room environment. Common ambient stimuli in the intermediate-care unit are background noise, light exposure, and nighttime nursing care. The archetypal patient with TBI in this setting will likely encounter blaring noise from intravenous (IV) pump alarms (Yoder et al., 2013), the constant presence of artificial light (Wenham & Pittard, 2009), or disruptions due to nocturnal repositioning or vital-sign checks (Inouye, 2013). These external factors can become noxious and impede optimal recovery (Duclos, Beauregard, Bottari, Ouellet, & Gosselin, 2015), especially since the cumulative effect of these nighttime awakenings perpetuate declines in neurological processing and daytime vigilance, even in the absence of brain injury (Bonnett, 2005; van Enkhuizen et al., 2014).

Although nighttime awakenings of intrinsic and extrinsic origin contribute to the patient's clinical disposition, external factors that derive from extrinsic origins have the potential to be readily remedied by nursing interventions; these factors can be linked to the immediate hospital environment (Elliott, Rai, & McKinley, 2014; Gabor et al., 2003).

Early nursing work by Parsons and Ver Beek (1982) and Falk and Woods (1973) helped to contextualize the importance of a patient's immediate care environment. Specifically, Parsons

and Ver Beek (1982) examined the influence of the ambient environment of the hospital room on the patient with TBI. Falk and Woods (1973) examined the hospital environment's influence on the non-TBI patient's well-being. However, the fact that the findings of both studies still inform the procedures of today's hospitalized patients with TBI show the salient and persistent nature of this problem.

Sleep in the Intermediate-care Patient with TBI

It is well documented that patients with TBI suffer from sleep disturbances (Ponsford & Sinclair, 2014; Watson et al., 2007). These include hypersomnia, insomnia, narcolepsy, somnolence (Ponsford et al., 2012), and circadian rhythm sleep disorders (CRSDs) (Ayalon, Borodkin, Dishon, Kanety, & Dagan, 2007). Most research on the sleep of patients with TBI focuses on the rest-activity behavior: arousal, alertness, attention, and sleep (Bushnik, Englander, & Katznelson, 2007; Kaushal, Ramesh, & Gozal, 2012). "Arousal" refers to the patients' ability to purposefully initiate social interaction, while "alertness" refers to their ability to respond to changes in the immediate environment within a reasonable amount of time ("reasonable" being relative to what people without a TBI would do). "Attention" refers to the patient's ability to sustain alertness within their environment. Finally, "sleeping" refers to patients' ability to cycle through the stages of sleep. Sleep comprises two main bio-physiologic processes; that is, rapid-eye movement (REM) and non-rapid-eye movement (NREM). The latter process itself comprises three stages: "N1", "N2," (light stages of sleep) and "N3" (deeper sleep or slow wave sleep).

The severity of TBI (mild to severe) is historically viewed as a predictor for sleep outcomes, though research does not always support this association (Duclos, Dumont, Wiseman-Hakes, et al. 2014). Results may vary because persons with mild or moderate brain injury are able to give a more comprehensive account of their sleep quality than their severely injured

counterparts (Viola-Saltzman & Watson, 2012; Wiseman-Hakes, Gaudreault, et al. 2013), especially when sleep is measured subjectively (Duclos, Dumont, Wiseman-Hakes, et al. 2014).

Objective measures like polysomnography (PSG) and actigraphy have also been used and provide strong evidence for sleep disturbances following TBI, such as decreased sleep efficiency, increased wakefulness after sleep onset (WASO), less REM sleep, and more slow-wave sleep (Shekleton et al., 2010; Makley, Johnson-Greene, Tarwater, Kreuz, Spiro, Rao, & Celnik, 2009). However, these studies do not address the sleep behavior of a patient with moderate to severe TBI who is housed on a neuroscience intermediate care specialty unit, and this is the gap this dissertation means to fill. Addressing this gap is important because delivery of care in the ICU differs from that in the intermediate care unit, and the patient with a severe or moderate TBI has a different clinical presentation and, subsequently, a different clinical acuity than a patient with a mild injury.

Although evidence suggests that sleep disturbances exist following brain injury (Watson et al., 2007; Bauman et al., 2007), most published literature has examined the sub-acute (e.g. 6–12 months; Baumann et al., 2007) or chronic (> 1 year) phase post-injury (Beaulieu-Bonneau & Morin, 2012). One of the few studies of sleep in persons with brain injury in the acute phase examined 16 patients in the ICU over ten days with moderate–severe injury (Duclos, Dumont, Blais et al., 2014). The authors in that study found associations with severe brain injury, higher disability levels, and poorer sleep architecture; however, they did not adjust for baseline disability, and it is unclear to what extent sleep disturbance and injury contributed to disability. Though Wiseman-Hakes et al. (2016), in their study of the onset of pervasive sleep-wake disturbances among ICU patients with severe TBI, conducted a PSG study (N = 7), it was cross-sectional and the sample consisted of ICU patients; however, it was shown that these patients had

an increased sleep duration and an earlier sleep onset. Chiu et al. (2013) and Chiu et al. (2014) use actigraphy on a neurological medical ward to map the trajectory of sleep (N= 52) and to also characterize the influence of sleep on injury severity and cognitive function (N= 52), but a majority of patients in both analyses had mild TBI. Both studies showed that patients with TBI had poor sleep architecture. In summary, examining sleep in this patient population is complex. Few studies have focused on the sleep of patients with moderate and severe TBI who are housed in a neuroscience specialty intermediate care unit.

Hospital-Related Environmental Stimuli

Disruptive stimuli can cause both physiologic and psychological harm to a hospitalized patient (Kamdar, Needham, & Collop, 2012; Inouye, 2006). Disruptive stimuli can also heighten a patient's need for pharmacological intervention and predisposes a patient to delayed healing (Alway, Halm, Shilhanek, & St Pierre, 2013). Environmental stimuli—a subset of disruptive stimuli—has been implicated as a main source of sleep disturbance among hospitalized patients (Buxton et al., 2012; Elliott et al., 2014; Pilkington, 2013). The physical constructs of environmental ambient stimuli—sound and light—have each been implicated in the literature as noxious to hospitalized patients (Buxton et al., 2012; Elliott, et al., 2014), with sound being the principal catalyst to sleep fragmentation (WHO Regional Office, 2009). One other plausible catalyst to nighttime awakenings in the hospitalized patient is movement of others, an ambient stimulus that is the result of care provision (Alway et al., 2013). In contrast to the aforementioned constructs of the physical environment, care provision is a construct of the social environment; in the dissertation it is operationalized as the around-the-clock bedside care that hospitalized patients often receive (Yoder et al., 2013) and is assessed as the movement of others in the room. How the movement of others is measured is described later in the dissertation.

There is profound heterogeneity in design, focus (intervention or descriptive), setting (laboratory or hospital), and methodology for the studies supporting the claim that the restorative quality of sleep among hospitalized patients is compromised by disruptive sound, light presence, and sporadic care provision (Wenham & Pittard, 2009; Buxton et al, 2012). Additionally, this quilt of heterogeneity does not include the phase of care where intermediate-care patients with TBI are housed and subsequently does not provide a comprehensive profile for the environmental stimuli this patient population may be subjected to. Examining the interaction of sleep and function in intermediate-care patients with TBI will assist in developing a profile of environmental stimuli that can be adapted to enhance recovery. Though studies of environmental stimuli that impact the patient with TBI in the intermediate-care phase of hospitalization are scarce, similar research questions have been answered in comparable phases of care, such as the ICU.

Gabor et al. (2003) used PSG on general ICU patients while simultaneously documenting sound pressure level and the number of patient-care activities. The healthy controls in their study were simply recruited to *stay* in the ICU. Peaks in sound pressure level were the main cause of awakenings in healthy controls. Conversely, neither background sound pressure levels (mean maximum levels during sleep were 60dB (A)) nor peaks in sound pressure level were statistically significant contributors to sleep disruptions in their ICU patients, despite evidence of poor sleep health (increased slow-wave sleep, excessive daytime sleep). An analysis of statistical associations between patient-care activities and sleep disruptions produced similar results.

Elliott et al. (2014) examined the relationship between disruptive sleep and what they call intrinsic (pharmacological interventions, pain from medical devices/procedures) and extrinsic (sound and light) factors among patients housed in the ICU. The researchers used PSG (PSG

sleep period time ratio) and several self-reported sleep instruments that also asked patients about their sleep before, during, and after their ICU stay. Elliott et al. (2014) found poor associations between most of the intrinsic and extrinsic factors of disruptive sleep and objective sleep recording (that is, PSG). Ironically, the presence of an artificial airway, an intrinsic factor, was the only factor that was associated with objective sleep; the presence of the airway was *positively* associated with objective sleep (that is, having the airway made sleep less disruptive to objective sleep). There was no association between subjective sleep measures and the intrinsic or extrinsic sleep disruptive factors. In this study, the median lux levels at night were ~1 and median sound pressure levels were 56 dB(A).

Alway et al. (2013) noted largely inconclusive results in their systematic review that examined sleep promotion interventions among ICU patients susceptible to ICU-acquired delirium. They included studies whose interventions were to give patients ear plugs to reduce sound perception and eye masks to reduce perception of light exposure. The results of the systematic review were inconclusive, owing to inconsistent instrumentation/measurement, dubious weighing of objective versus subjective results for sleep parameters, varied study settings, and varied disease processes of subjects.

While studies from ICU settings are helpful in identifying factors that would influence sleep, new approaches are needed when considering environmental stimuli pertinent to the intermediate-care patient with TBI. Specifically, each environmental variable mentioned—sound, light, and care-provision—needs to be discretely measured in this patient population because each of these environmental variables has been cited as a problem in hospitalized populations (Buxton et al., 2012; Elliott et al., 2014; Gathecha et al., 2016; Giménez et al., 2017). However, to date, there are few, if any, studies that have examined the discrete influence

of each factor on nighttime awakenings in a single study. Further, the profile for ambient stimuli among the intermediate-care patient with TBI may prove to be drastically different from that of their ICU counterparts with regard to sound, light, and care-provision variability (Schneider & Pomidor, 2014). Before developing interventions to improve sleep for this patient population, it is imperative to fully characterize these variables.

Conceptual Framework

The current investigation draws from principles outlined in the Human Ecology Model (Bubloz & Sontag, 1993). The concepts of environment, human, and interaction correspond respectively with the intermediate-care setting, the patient with TBI, and the interactions between patient and environment. This study is based on the interplay between the patient with TBI and the intermediate-care setting; specifically, the influence of nighttime awakenings on functional outcome. Nighttime awakenings are used in the study as the primary outcome measure of sleep. It is hypothesized that those with fewer nighttime awakenings will have better function at time of discharge (as measured by the functional independence measure, FIM ®) than those with more awakenings.

Assessing the environment of care and its influence on patients with TBI in the neuroscience specialty intermediate-care unit is important because it can uncover mutable practices that inhibit sleep and that can undermine functional recovery. Unfortunately, to date there is limited published information that attempts to characterize the sound, light, and care provision for the intermediate-care patient with TBI and how these qualities impact sleep and functional outcome. Furthermore, discretely assessing the environmental variables simultaneously with sleep would allow for inferences about the association between

environmental stimuli and nighttime awakenings. This dissertation addresses those gaps in knowledge.

STATEMENT OF STUDY PURPOSE

The three main objectives of the dissertation are as follows:

- 1) To describe the number of documented nighttime care events to patients housed on a neuroscience intermediate care unit; and to examine the association between the average number of documented nighttime care events and the proportion of nights that the nurse's note said that the patient "slept well"
- 2) To describe the sleep profile of patients with a moderate or severe TBI who are housed in a neuroscience intermediate care unit; and to describe the association between the patient's injury severity and their sleep parameters. Additionally, it was important to describe how disturbed sleep may impact the patient's functional outcome at the end of their hospital stay.
- 3) To describe how the combined contribution of ambient stimuli (sound, light, and the patient-care interventions (a variable that will be indirectly assessed by movement of others in the patients room) impacts the probability of nighttime awakenings in patients who were housed on a neuroscience intermediate care unit; and to describe whether the relationship between the ambient stimuli (sound, light, and movement of others) and sleep varies with the patient's night of stay in the hospital.

Dissertation Chapters

There are five chapters of this dissertation, but unlike a monograph, it will be an article-based dissertation. The article-based dissertation is also known as the "compilation thesis" (Gustavii, 2012, p. 3) and comes in two forms: the Scandinavian model and the sandwich format. The current dissertation will use the latter form, in which the articles appear as chapters and are

sandwiched between an introduction (Chapter 1) and a general discussion (Chapter 5). Therefore, Chapters 2, 3, and 4 will be modeled after articles written for scientific journals. Specifically, Chapter 1 outlines the significance of the research problem, the pertinent background literature, and the statement of purpose. Chapter 1 also prepares the reader for what is to come in the following four chapters.

Chapter 2 reports the findings from a retrospective chart review of the electronic medical record (EMR) notes of bedside clinicians who cared for patients with moderate and severe TBI. This chapter includes a descriptive analysis of patient characteristics, activities conducted during the nighttime hours of care, and the proportion of nights that the nurse's note said that the patient had "slept well." The data in Chapter 2 was extracted between January 2013 and March 2013 is from an independent study the author conducted where the sample was (N = 34). This distinction is important because the data used in Chapter 3 and Chapter 4 are from a different independent study where data was collected between June 2016 and January 2017. For Chapter 3, the sample was (N = 17) and for Chapter 4, the sample was (N= 18).

Chapter 3 reports findings from a single cohort feasibility study design (N=17) that used actigraphy—an instrument that renders rest-activity cycles comparable to sleep-wake cycles from PSG (Ancoli-Israel et al., 2003)—to obtain objective sleep data from patients hospitalized with a moderate or severe TBI. The sleep parameters analyzed were wake bouts, total wake time, and sleep efficiency. Scores from the functional independence measure (FIM) ® and other disability/injury severity scales were also collected. This study presents descriptive findings on the sleep patterns of hospitalized patients with moderate or severe TBI, functional outcome of these patients, and the strength of associations that exist between sleep parameters and disability/injury severity variables.

Chapter 4 also reports findings from a single cohort pilot study; however, the sample was (N= 18). Moreover, the findings demonstrate the pattern of ambient stimuli (sound, light, and movement) in the hospital rooms of patients with moderate and severe TBI. The study presents descriptive findings on ambient stimuli, its pattern of exposure after longitudinal collection (Neitzel, Stover, & Seixas, 2011), and the influence of each of these stimuli on nighttime awakenings in this patient sample.

A brief synthesis of the main points from each paper is included in Chapter 5. This chapter makes a cohesive presentation of the impact of ambient sound, light, and movement of others on the hospitalized patient with TBI, a discussion on the use of novel sensor technologies to measure longitudinal environmental data, and methodological considerations for future research.

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CHAPTER 2

Sleep of Intermediate Care Patients with TBI: Role of Nursing Activities during Nighttime Hours

Abstract

BACKGROUND: Sleep disturbance is a problem for patients with traumatic brain injury (TBI). For patients housed in the hospital in a non-ICU setting, nighttime nursing care activities can be a main factor in how well a patient may sleep. **AIMS:** This study aimed to describe the documented nighttime care provision to intermediate-care patients with TBI. The study also aimed to examine the relationship between average number of documented nighttime nursing care activities and the proportion of nights patients were documented as having slept well.

METHODS: Retrospective chart review study. Subjects were identified from the trauma registry as being hospitalized following a moderate-severe TBI between January and March 2013. Data were extracted from the electronic medical record (EMR). The variables of “mean nighttime care activities” and “slept well” were created from nursing notes in the EMR and were recorded for patients between 2200 and 0800 HRS for up to 7 days. Demographic and injury variables were also extracted. Data analysis included descriptive statistics, bivariate correlations, and simple regression analyses. P -values ≤ 0.05 were considered statistically significant.

RESULTS: There were 34 subjects that met inclusion criteria. Initial mean GCS was 4.1 and average length of stay was 5.9 days. Sleep/rest was poorly captured in the nursing documentation. The mean number of nighttime care activities per patient was 5.6. Patients were

reported to have slept well for only 16% of the nights they were housed on the unit. Pearson's r for correlation between nighttime care activities and sleep quality was weak. **CONCLUSIONS:** A standard way of capturing sleep/rest within the medical record needs to be developed to allow for better documentation and nursing care planning. Further research is needed in this understudied phase of care to better gauge the factors that influence sleep disturbances.

Keywords: acute care, sleep, brain injury, nursing care

INTRODUCTION

According to the most recent epidemiologic reports, 2.8 million adults in the United States suffered a traumatic brain injury (TBI) in 2013. Of these people, 282,000 required hospitalization (Taylor, Bell, Breiding, & Xu, 2017). The frequent monitoring and surveillance that occurs during hospitalization can create a care environment that is not always supportive of recovery. The care environment that will be the focus of this investigation is that of the neuroscience specialty intermediate care unit--the phase of hospitalization which follows the neurological intensive care unit (ICU); the former is often referred to as the neuro-acute-care unit or the neuro-*floor*.

Sleep is known to be an important behavior for recovery from injury and has only recently been explored in the hospitalized patient with TBI (Chiu, Chen, Chen, Chuang, & Tsai, 2013; Duclos et al., 2014). Sleep patterns need to be further explored among the target patients housed in the neuroscience specialty intermediate care unit because as the last phase of in-patient hospitalization, it is a critical juncture for evaluating functional outcomes (Schumacher, Walder, Delhumeau, & Müri, 2016). Although, sleep has been shown to be a reliable indicator of functional outcomes in the hospitalized patient with moderate and severe TBI (Sandsmark et al., 2016), to date, and to our knowledge, only two studies have assessed the sleep of this target population in an *intermediate-care* setting. While the studies that assessed the sleep of this target population in an ICU setting are valuable contributions to the body of literature, the patient care that is administered in the neurological ICU is different from that of the neuroscience specialty intermediate care unit with regard to workflow, workload, and responsibility of nursing staff (Nelson, Valentino, Iacono, Ropollo, Cineas, & Stuart 2015). This difference in patient care

delivery suggests the neuroscience specialty intermediate care unit is a novel research environment that requires its own evidence.

While housed in an intermediate-care unit, the patient may not only experience sleep disturbances brought on by their injuries, but also by the care environment itself (McNett, Sarver, & Wilczewski, 2012). Sleep disturbances in this population arise from both intrinsic and extrinsic factors (Watson, Dikmen, Machamer, Doherty, & Temkin, 2007; Yoder, Yuen, Churpek, Arora, & Edelson, 2013) and greatly contribute to functional outcomes. Sleep disturbances are pertinent to hospitalized patients with moderate and severe TBI because; of their inability to maintain restful sleep (intrinsic in origin) (Duclos et al., 2014) and the increased likelihood of being awakened from their sleep owing to patient-care related interruptions (extrinsic in origin) (Yoder et al. , 2013). Both of these conditions highlight the multifactorial nature of sleep disturbances in the hospitalized patient with moderate and severe TBI.

In patients following TBI, intrinsic sleep disturbances are believed to be caused by damage to brain circuitry responsible for regulating sleep and wakefulness (Viola-Saltman & Watson, 2012). Extrinsic factors, conversely, are a direct result of disruptions that are common in the environment, including ambient noise, light exposure, and nighttime nursing care activities. Nighttime nursing care can compound the sleep disturbances that are precipitated by intrinsic sources (Alway, Halm, Shilhanek, & St Pierre, 2013; Yoder et al., 2013) and may be especially problematic for patient recovery following TBI (Massengale, 2015). The purpose of our study was to examine a potential relationship between the nurses' nighttime care-provision to patients with moderate and severe TBI and the nurse's documentation of the patients' sleep quality. Demographics and injury variables of the intermediate-care patient with severe TBI are

discussed, nurse-driven nighttime care activities are identified, and implications for practice are noted.

Related Literature

The ideal caregiving environment is one that facilitates useful interaction with the patient and one that facilitates healing (Stichler, 2001). An essential element of professional nursing practice is the maintenance of an environment of care conducive to healing and optimal recovery. In exploring some of the causes for sleep disturbance in hospitalized patients, environmental stimuli have been implicated as a main source (Buxton et al., 2012; Elliott, Rai, & McKinley, 2014; Pilkington, 2013). Nighttime care provision has been identified as a noxious stimulus and a cause for sleep disturbance. For example, the typical patients with TBI in this setting will likely encounter interruptions due to nightly repositioning, vital sign checks, or neuro-checks (Inouye, 2013).

Among the studies that examined sleep among intermediate-care patients with TBI (Chiu et al., 2013; Chiu, Lo, Chiang, & Tsai, 2014), though conditions were not characterized as part of their investigation, the hospital environment was *noted* as a precipitating factor in sleep disturbance. While essential, excessive nighttime provision can impede optimal sleep (Duclos, Beauregard, Bottari, Ouellet, & Gosselin, 2015) and potentially decrease neurological processing and daytime vigilance (Bonnett, 2005; van Enkhuizen, Acheson, Risbrough, Drummond, Geyer, & Young, 2014). Unfortunately, to date, there is limited published information on care provision to intermediate-care TBI patients, much less care provision to these patients during the nighttime hours. Also lacking in the literature is an analysis of nursing documentation done during the nighttime hours for these patients. This study aimed to address these gaps by providing a better

understanding of nighttime care provision for severely injured TBI patients housed in the neuroscience specialty intermediate-care unit and the relation of that care to sleep quality. This study sought to understand how documented nighttime care provision corresponds with documented sleep reports in this patient sample.

AIMS

The specific aims of this study were to: 1) describe the documented nighttime care provision to neuroscience specialty intermediate care patients with TBI; 2) examine the relationship between average number of documented nighttime care activities and the proportion of nights patients were documented as having slept well.

METHODS

This was a retrospective chart review study and was the first step in a program of research examining sleep and environment in TBI patients. A list of patients with ICD-9-CM diagnoses of TBI hospitalized at a level 1 trauma center between January and March 2013 was provided to the PI by the trauma registry to allow for screening against eligibility criteria. The interval of January to March was selected so that one full quarter the year was collected. Furthermore, this interval was based on numbers of patients admitted to the hospital with moderate and severe TBI. During this period of data collection, there were no ongoing quality improvement sleep hygiene campaigns. Institutional review board (IRB) approval was received from the University of Washington (UW) for this medical record study.

Subjects

Eligibility criteria for subjects: 1) Admitted to between January-March 2013 with ICD9-CM diagnosis of TBI (codes 800.0-801.9, 803.0-804.9, 850.0-854.1, or 959.01); 2) Initial Glasgow Coma Scale score (GCS) on Admission to the Emergency Department (ED) of ≤ 8 ,

indicating severe brain injury (Jenett & Teasdale, 1977). Subjects were excluded if they spent less than 24 hours on the neuro intermediate care unit or died during the first seven days on that unit.

Screening

Of the 83 patients initially identified by the trauma registry, 34 met the eligibility requirements and were included in the study.

Demographic Variables

Demographic information was extracted from the electronic medical record (EMR) and included age, gender, race, ethnicity, insurance coverage, length of stay (LOS) on the neuro-unit, and marital/partnered status. Civil unions and common law marriage were recognized as partnered.

Injury Variables

The GCS score from the initial physician's note on admission to the ED came from the EMR, while the Injury Severity Scale (ISS) score came from the trauma registry. The ISS is a measure designed to reflect the extent and overall intensity of an individual's bodily injuries (Baker, O'Neil, Haddon & Long, 1974; Baker & O'Neil, 1976). The ISS ranges from 1 (least severe) to 75 (most severe) with higher scores indicating greater likelihood of mortality (Baker & O'Neil 1976).

Nightly Caregiving

Nursing activities carried out between the hours of 2200 and 0800 were identified as nighttime care activities. The time interval of nighttime care was selected based on the combined clinical experience of the authors. It was agreed that this time interval is when patients were

expected to be sleeping, preparing for sleep, or emerging from sleep. These activities included toileting the patient, providing oral care, patient hygiene, turning the patient, and giving medications. Though not exhaustive, these care activities are common among neuroscience specialty intermediate care unit patients with severe TBI who are generally unable to provide self-care (Nelson et al., 2015). Each activity was extracted from the EMR for either the first seven days the patient was housed on the unit, until the patient was discharged from the unit, or until the patient was transferred to a higher level of care (ICU) for unforeseen complications. In any event, the data from the patient were still used.

Subsequently, the five nighttime care activities were averaged over each patient's *respective* days of data collection on the unit. For example, if a patient was on the unit for three days and then was transferred to the ICU owing to complications, their nighttime care activities were averaged over 3 days. This data was then collapsed into a single category that gave an average of all nighttime care activities. This average of all care activities was named "mean nighttime care activities" and reflected the specific LOS for each of the 34 patients. Though taken much later than the period of data extraction, Figure 2 shows the hallway view of a room of a patient with TBI housed on this unit during the nighttime hours.

Sleep Variable

A binary questionnaire ("Yes/No") was used to extract data from the EMR-based, nurses' end-of-shift summary. This questionnaire asked whether or not the patient slept well. "Yes" was recorded if there was explicit documentation in the summary by the nurse that the patient slept well or slept well through the night. "No" was recorded if there was documentation that the patient did not sleep well or slept poorly. Accounts of patient "currently resting" were not included in the analysis because these statements do not explicitly speak to the quality of sleep.

If there was no report of whether the patient had or had not slept well, then an “unknown” response was recorded.

Data Analysis

SPSS 19.0 (IBM, Armonk, New York) and [R]Studio (3.3.1) were used to manage and analyze the data. Data analyses included descriptive statistics, bivariate correlations, and simple regression analyses. A p -value ≤ 0.05 was considered statistically significant.

Controlling for Confounding Variables

Given that the authors were interested in nursing care as the independent variable, rather than patient factors, controlling for age was not appropriate in this context. As such there should be no difference in care activities based on age alone. Also, given that the dependent variable—“slept well”—was the documented account of the night-shift nurses’ end-of-shift-summary, there is no evidence to support that the dependent variable would change with the statistical controlling of age. For objective measures of sleep (actigraphy/ polysomnography), controlling for age and other patient factors would be appropriate, however, in this context of patients with TBI, it is not appropriate to consider. Conversely, future studies should control for these patient factors when looking at objective measures of sleep (Arnardóttir, Thorsteinsson, & Karlsson, 2010).

Correlation

To see if there was a relationship between the percent of nights the patient was documented as sleeping well (dependent variable) and the mean nighttime care activities (independent variable), a correlation (zero-order) was conducted. This statistic ranges from +1 to -1 and values closer to either of the numbers indicate a strong relationship between the variables being compared.

Simple Regression

A simple regression analysis was conducted to see if mean nighttime care could predict the percent of nights the patient was reported as sleeping well.

RESULTS

Characteristics and Demographics

Of the study sample ($n=34$), 88.2% were male ($n=30$), 79.4% were white ($n=27$), and the average age was 46 years old. (see Table 1 for details on sample characteristics and demographics). Figure 1 shows a scatter-plot of individual observations for each of the 34 patients. The entire sample was documented as sleeping well for less than half ($< 50\%$) of the nights they were housed on the neuroscience specialty intermediate care unit.

The mean nighttime care activities range from 0 to 10; this means that some patients received as many as 10 care-activities on a given night. The average number of nighttime nursing care activities (Table 2) administered between the hours of 2200 to 0800 was 5.6.

Correlation & Regression

Table 3 shows the output from the zero-order correlation. The Pearson r between documented sleep quality and mean nighttime care was weak ($r = 0.05$). Conversely, Table 4 shows the Pearson r when medications are not included as a care activity.

Table 5 shows the regression model which suggests that, given the mean amount of nighttime care activity, patients in this sample were expected to sleep well for about 16% of the nights they were housed on the unit; that is, about 1-2 nights in the first week. Table 6 shows what the regression model would look like without medication included as a care activity. Furthermore, the percent of nights the patients slept well can be expected to increase by 0.05% for each additional care activity.

DISCUSSION

Main Findings

The main results of this study suggest that there was not association between mean nighttime care activities and the nurses' documentation of the patients sleep quality. Furthermore, nighttime care activities from the EMR did not seem to be a reliable predictor of the patient's sleep quality (which was also based on the nurses' end-of-shift summary). Based on descriptive statistics and sample characteristics, patients in this study were similar in their demographics to other published studies of hospitalized TBI patients (Chiu et al., 2013a; Susman et al., 2002; Udekwu, Kromhout-Schiro, Vaslef, Baker, & Oller, 2004).

No Relationship between Mean Nightly Care activities and Sleep Quality

This finding was likely related to the limited documentation of sleep quality found in the EMR. Our findings of "no relationship" and "no clinical significance between the documented accounts of sleep quality and documented nighttime nursing activities" were consistent with results of a study done by Ugras and colleagues (2015) where the frequency of nocturnal patient care activities and reports of patient's sleep disturbance in a neurosurgical ICU were not statistically significant. The care activities included in our analysis were similar to those used in the Ugras et al. 2015 analysis.

Unlike our study, Ugras et al. (2015) developed their own questionnaire for collecting the patient's sleep quality and collected data in a prospective manner. The studies by Ugras and colleagues (2007, 2015) also focused on ICU patients, thus our study extends available knowledge to intermediate care patients in neuroscience specialty units. A study of (non-TBI) intermediate care patients (n=108) in a tertiary, general-ward hospital also failed to find a statistically significant difference between the patients' report of being sleep deprived and

environmental/health personnel related factors (Shafiq et al., 2006). Some of the reasons cited for that is result include: investigating the patient's sleep only during the night, the patient's recall bias, and patient's attitudes and expectations of care (Shafiq et al., 2006).

A drawback to the retrospective chart review is that we could not account for the quality of information initially entered in the chart. However, results from a study by Ritmala-Castren, and colleagues, (2014) showed that patient's report of sleep quality and nurse documentation of sleep corresponded only about 57% of the time. In that study, nurses documented the overall quality of the patient's sleep for just 27% of the patients (n = 114)—a result that was similar to our report. Both the study by Ritmala-Castren et al. (2014) and this study reinforced the need for better documentation of sleep quality in the medical record. This could be accomplished with a specific item in the flowsheet and may heighten nurse's awareness of the importance of sleep for hospitalized patients. Interestingly, data from time and motion study of night-shift nurses (Desjardins, Cardinal, Belzile, & McCusker, 2008) suggests night-shift nurses spend significantly more time on indirect care, including documentation, compared to their evening-shift and day-shift counterparts. Thus, the quality of documentation would be expected to be better on the night-shift. Furthermore, based on the available documentation, we were unable to tell who initiated certain care activities like toileting.

That there was not association between mean nightly care activities and sleep quality may also be due to the way we chose to define and quantify nursing activities. Though we could not identify a standard tool to quantify nursing care in an intermediate hospital setting, a modified use of the ICU-specific nursing activities score (NAS) may have been an alternative approach (Miranda, Nap, de Rijk, Schaufeli, Iapichino, & TISS Working Group, 2003; Reis-Miranda & Jegers, 2012). The types of nursing activities we selected may have also been an issue.

Medication administration carries a mild weight per the NAS (Miranda et al., 2003). The heterogeneity in how researchers capture what hospital nurses do generally (Reis-Miranda & Jegers, 2012) and what hospital nurses on *night shift* do (Nelson et al., 2015) can be a problem for the development of environment of care interventions. Another limitation was that sleep quality was not assessed with a gold standard measure like actigraphy or polysomnography, and is an area for future research.

Strengths of this study were that its methods and analyses can be implemented and conducted with relative ease. Seamless and parsimonious methodologies are important when initiating research in patients associated with an understudied phase of care like those described here (patients with moderate and severe TBI). Moreover, this study added to the growing body of literature concerning sleep and health outcomes of patients hospitalized with TBI by showing the frequent occurrence of patient-care activities during nighttime hours. Where previous work in this target population has focused on sleep disturbances in the ICU/critical care phase, with this study, we were able initiate a discourse about those housed on a neuroscience specialty intermediate-care unit.

Clinical Implications

Despite overwhelming evidence that patients with TBI have trouble sleeping (Ouellet, Beaulieu-Bonneau, & Morin, 2015a), further studies need to be done to uncover the mutable causes among severely injured, hospitalized sub-populations. Even if documentation of patient sleep may not be widely practiced in some hospital organizations (Meissner, Riemer, Santiago, Stein, Goldman, & Williams, 1998; Ritmala-Castren et al., 2014), improved documentation could benefit the intermediate-care patient with TBI (Gearing, Olney, Davis, Lozano, Smith, & Friedman, 2006) given the known influence of quality sleep on cognition and functional

outcomes (Sandsmark et al., 2016). Intentional documentation of patient sleep quality may cause the health-care team to pay closer attention to hospital factors that influence the patient's sleep health (Griffith, Thompson, Rathore, Jehi, Tesar, & Katzan, 2015; Hillestad et al., 2005). Closer attention to the environmental factors that may influence the sleep health of patients with TBI may challenge the health-care team's perception that sleep disturbances in these patients are unmodifiable (Alway et al., 2013; Yoder et al., 2013). This may allow for bedside nurses to advocate for sleep promoting environment-of-care changes in a more impactful way. Moreover, a standard method of assessing, diagnosing, planning, implementing, evaluating and documenting sleep health should be a part of this initiative (Enomoto et al., 2010; Fanfulla, Ceriana, D'Artavilla- Lupo, Trentin, Frigerio, & Nava, 2011). More empirical research studies need to be conducted on this group so that pertinent guidance about documentation of sleep/rest can be enacted; this guidance can better inform nursing interventions to promote sleep health and improve overall quality of life while in the hospital.

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Tables

Table. 2.1
Demographic Characteristics of Intermediate care Patients with TBI on Neuroscience Unit (N=34)

Measure	<u>n</u>	<u>%</u>
Male	30	88.2
White	27	79.4
Marital status: Single	16	47.1
Marital status: Married	14	41.2
Had health insurance	22	64.7
	<i>M</i>	<i>SD</i>
Length of stay on unit (days)	5.91	1.78
Glasgow Coma Scale Score (GCS)	4.09	1.96
Injury Severity Score (ISS)	29.18	16.13
Functional Independence Measure (mFIM)	7.62	3.06
Patient Age	46.68	18.32

Note. The GCS used for this study was obtained from initial physicians note in the emergency department.

Table 2.2.
The Study Samples' Documented Care Activities per Night (N=34)

Measure	<i>M</i>	<i>SD</i>	<i>Min.</i>	<i>Max.</i>
Toilet	1.7	1.1	0	4.0
Turns	1.5	1.0	0	3.6
Bath	1.2	0.9	0	4.0
Medication	1.0	1.2	0	6.7
Oral	0.2	0.4	0	1.4
Total	5.6	4.6	0	19.7

Table 2.3.
Zero-Order Correlations Including Medication as a Nighttime Care Activity (N=34)

Measure	<i>M</i>	<i>SD</i>	1.	2.
Outcomes				
1. Reports of sleeping well	0.2	(0.2)	--	
Predictors				
2. Mean of nighttime care activities	5.6	(2.4)	.05	--

Note: Report of sleeping well is a proportion, but is treated as a percentage in the body of this article; *p*-value = 0.8.

Table 2.4.
Zero-Order Correlations Excluding Medications as a Nighttime Care Activity (N=34)

Measure	<i>M</i>	<i>SD</i>	1.	2.
Outcomes				
1. Reports of sleeping well	0.2	(0.2)	--	
Predictors				
2. Mean of nighttime care activities	4.5	(2.8)	-.08	--

Note: Report of sleeping well is a proportion, but is treated as a percentage in the body of this article; *p*-value = 0.6

Table 2.5.

Simple Linear Regression for Percentage of Nights Patients Slept Well and Mean Nighttime Care Including Medication Administration (N=34)

	R^2_{total}	$R^2_{adjusted}$	$F(1,32)$	p	b	(SE)	$t(32)$	p
<i>Report of slept well</i>	0.002	-0.03	0.09	.765				
Intercept					0.16	(0.09)	1.70	.09
Mean nighttime care w/ RX					0.004	(0.02)	0.30	.765

Note. Mean nighttime care activity is an average of nursing care activities completed between the hours of 2200-0800. Reports of "slept well" is the percent of nights (here listed in proportion form) a patient was documented as having slept well. Predictors were not standardized for analysis. RX is short hand for medications.

Table 2.6.

Simple Linear Regression for Percentage of Nights Patients Slept Well and Mean Nighttime Care Excluding Medication Administration (N=34)

	R^2_{total}	$R^2_{adjusted}$	$F(1,32)$	p	b	(SE)	$t(32)$	p
<i>Report of slept well</i>	0.007	-0.024	0.23	.634				
Intercept					0.22	(0.07)	2.97	.006
Mean nighttime care					-0.007	(0.01)	-0.48	.634

Note. Mean nighttime care activity is an average of nursing care activities completed between the hours of 2200-0800. Reports of "slept well" is the percent of nights (here listed in proportion form) a patient was documented as having slept well. Predictors were not standardized for analysis.

Figures

Figure 2.1. Scatterplot of Mean Nighttime Care Activities and Percentage of Nights with Good Sleep

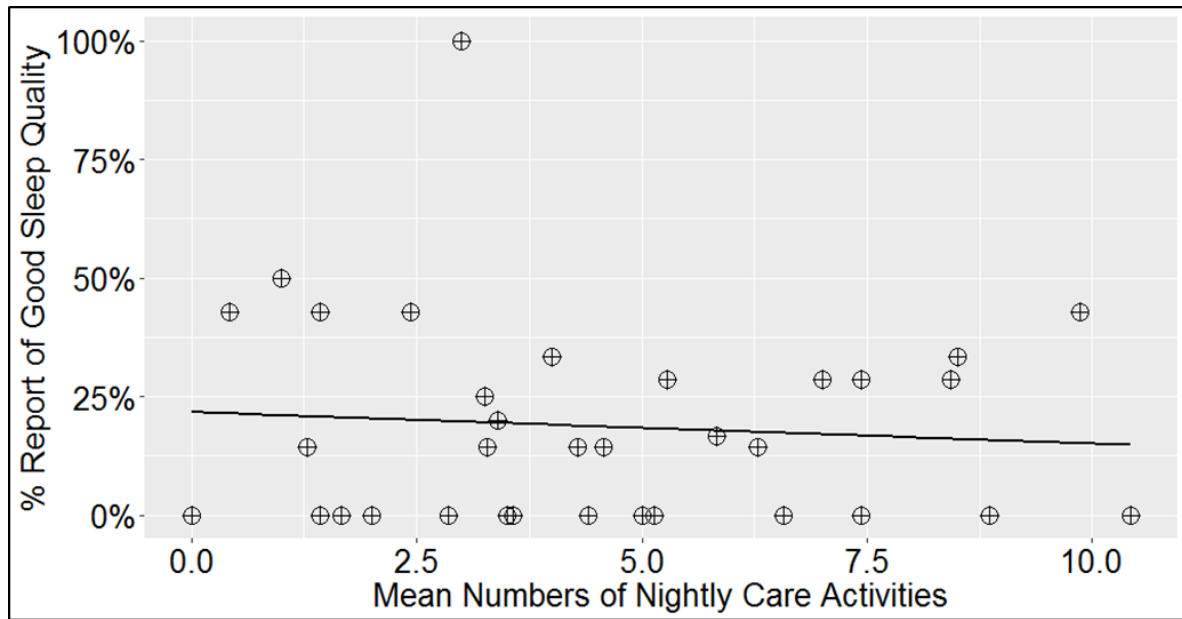


Figure 2.2. Photo of an occupied hospital bed at night on the neuroscience intermediate care specialty unit (photo credit Ellita T. Williams, 2016).



CHAPTER 3

Examining the Feasibility and Measurement of Nighttime Sleep Disturbances and Outcomes at Discharge in Patients with TBI Housed on the Neuroscience Specialty Unit

Abstract

BACKGROUND: Patients with traumatic brain injury (TBI) are subject to sleep disturbances resulting from their injury and the environment of care. To date, there has been little examination of sleep among hospitalized patients with moderate and severe TBI on acute care specialty units; as well as understanding the role of sleep quality on patient outcomes. **AIMS:** 1) address feasibility of collecting sleep data in patients with moderate to severe injury that are housed on a neuroscience unit; 2) describe sleep patterns as it relates to injury characteristics; and 3) to examine the relationship between sleep quality and patient outcomes at discharge. **METHODS:** Subjects recruited from a neuroscience specialty unit in a level-1 trauma center (N=17) wore wrist actigraphy for up to five consecutive nights. Rest-activity cycles were examined by wake bouts (#), total wake time (in minutes), and sleep efficiency (%) and were evaluated during the nighttime sleep periods. Subjects were administered the Rancho Los Amigo scale (RLA) at study entry and the functional independence measure (FIM) at hospital discharge. Injury variables obtained were Glasgow coma scale (GCS) score and injury severity scale (ISS). Variables were entered as a fixed effect in a multi-level linear regression model [(RStudio version 3.3.1)]. Bayesian inference criterion (BIC) and ANOVA was used to determine the best model fit. Multiple linear regression was used to assess the subjects' aggregated sleep parameters against FIM. **RESULTS:** The subjects' mean age was 63.4 (SD= 17.9) and average GCS was 8.8 (SD =

4.9). 10 of 17 subjects had a subdural hematoma. Average sleep efficiency across all nights assessed was abnormal at 73% (SD = 15). The average wake bout and total wake time were abnormal at 41 (SD = 18) and 74 minutes (SD = 47), respectively. RLA proved to be a strong predictor of wake bouts ($\chi^2(1) = 4.44, p = 0.04$). None of the sleep parameters could reliably predict functional outcome at discharge. **CONCLUSION:** Collecting rest-activity data on this target population is feasible. Future investigators should consider quick patient turn-around, presence of legally authorized representative and language barriers. Overall, it seems patients with TBI are have disturbed nighttime sleep during their hospitalization. Also, their level of cognitive functioning can inform anticipated wake bouts. ISS and GCS did not seem to make predict sleep disturbances. While nothing can be done to change the state of the patient's injury, nighttime hospital staff (including nursing) can help to normalize sleep disturbances (decreasing wake bouts and total wake time; increasing sleep efficiency) among patients with higher cognitive functioning.

Key Words: neuroscience specialty unit, actigraphy, traumatic brain injury, outcome.

INTRODUCTION

Nearly 300,000 people were hospitalized for TBI in the US in 2013 (Taylor, Bell, Breiding, & Xu, 2017). Patients with moderate or severe TBI are most likely to require hospitalization, and managing these more complex cases of TBI is resource intensive to hospitals (Fountain, Kolia, Laing, & Hutchinson, 2016). While TBI has a complex arrangement of symptoms that accompany the injury, poor sleep has been cited as an important behavioral disturbance (Parcell, Ponsford, Rajaratnam, & Redman, 2006; Ponsford & Sinclair, 2014; Wiseman-Hakes et al., 2016). Complexity is added when patients with moderate and severe TBI are expected to engage in restful sleep behavior in a hospital setting.

Sleep is known to be an important behavior for recovery from injury and has only recently been explored in the hospitalized patient with TBI (Chiu, Chen, Chen, Chuang, & Tsai, 2013; Duclos et al., 2014). However, the sleep behavior of patients housed on a neuroscience specialty unit requires further exploration as this is often the last place patients are cared for in the hospital before they are discharged. This original research article reports on the sleep/wake parameters of patients with moderate and severe TBI and how sleep parameters relate to function.

BACKGROUND

Many patients with TBI are subject to sleep disturbances as a result of damage to neural networks responsible for regulating sleep-wake cycles; mainly, mechanical insults to the cerebral cortex, subcortical structures and surrounding structures (Viola-Saltzman & Watson, 2012; Kumar et al., 2009; Bauman et al., 2005). Sleep disturbances in patients with TBI typically manifest as dyssomnias and parasomnias (Mazwi, Fusco, & Zafonte, 2015; Nakase-Richardson et al., 2013).

Most of the research done concerning the sleep of patients with TBI focuses on the hallmarks of rest-activity behavior in patients with TBI: alertness, attention, sleep, and arousal (Bushnik, Englander, & Katznelson, 2007; Kaushal, Ramesh, & Gozal, 2012). The severity of TBI (mild to severe) is historically viewed as a predictor for sleep outcomes, though research does not always support this association between severities of injury and sleep disturbance (Duclos, Dumont, Wiseman-Hakes, et al. 2014). Varied results may exist because persons with mild or moderate brain injury are able to give a more comprehensive account of their sleep quality than their severely-injured counterparts (Viola-Saltzman, 2012; Wiseman-Hakes et al., 2013); especially when subjective measures of sleep are utilized (Duclos, Dumont, Wiseman-Hakes, et al. 2014).

Objective measures like polysomnography (PSG) and actigraphy have also been utilized and provide strong evidence for sleep disturbances following TBI such as decreased sleep efficiency, increased wake after sleep onset (WASO), less REM sleep, and more slow-wave sleep (Shekleton et al., 2010; Makley, Johnson-Greene, Tarwater, Kreuz, Spiro, Rao, & Celnik, 2009). However, these studies do not address the sleep behavior of a patient with moderate to severe TBI who is housed on a neuroscience specialty unit. Addressing this gap is important because the care delivery in the ICU is different from that of the intermediate care unit, and the patient with a severe or moderate TBI has a different clinical presentation and subsequently, a different clinical acuity than a patient with a mild injury.

Although evidence suggests that sleep disturbances exist following brain injury (Watson, Dikmen, Machamer, Doherty, & Temkin, 2007; Bauman, Werth, Stocker, Ludwig, & Bassetti, 2007), most published literature has examined the sub-acute (e.g., 6-12 months; Baumann et al.,

2007;) or chronic (> 1 year) phase post-injury (Beaulieu-Bonneau & Morin, 2012). One of the few studies to date of sleep in persons with brain injury in the acute-phase examined 16 patients over 10 days in the ICU with moderate-severe injury (Duclos, Dumont, Blais et al., 2014). The authors found associations with severe brain injury, higher disability levels and poorer sleep architecture; however, they did not adjust for baseline disability, and it is unclear to what extent sleep disturbance and injury contributed to disability. Though Wiseman-Hakes et al. (2016) conducted a PSG study (N = 7) on patients with severe TBI, it was cross-sectional and the sample consisted of ICU patients. Chiu et al. 2013 and Chiu et al. 2014 used actigraphy on a medical ward to map the trajectory of sleep (N= 52) and to also characterize the influence of sleep on injury severity and cognitive function (N= 52), but a majority of patients in both analyses had mild TBI.

In sum, examining sleep in this patient population is complex. Few studies have examined sleep in TBI patients, and even fewer studies have focused on those in intermediate-care (Chiu, Chen, Chen, Chuang, & Tsai, 2013b; Chiu et al., 2014) What also remains unclear is the relationship between outcome and quality of sleep among patients with moderate and severe TBI. Results from a study that evaluated sleep behavior with continuous electroencephalogram (cEEG) in this patient population showed that poor sleep was predictive of poor outcomes in rehabilitation settings (Sandsmark et al., 2016); another study showed that for patients with mild TBI, poor sleep was predictive of subacute (1- 6 months post injury) concussive symptoms (Sullivan, Berndt, Edmed, Smith, & Allan, 2016) . Although neither study focused on the patient population housed in the intermediate care setting of hospitalization, they lend evidence to the impact that sleep disturbances could have on outcomes in patients with TBI.

PURPOSE

Therefore, understanding the sleep patterns of this patient population is important. The purpose of this study is to report on the feasibility of collecting sleep data in this group and to describe sleep and injury characteristics.

AIMS

There are 4 aims to this study:

1. Describe the feasibility of measuring sleep/wake in a sample of hospitalized moderate-severe TBI patients using actigraphy.
2. Describe the sample's sleep parameters in terms of wake bouts (counts), sleep efficiency (%), and total wake time (in minutes).
3. Explore the relationship between injury characteristics and sleep parameters.
4. Explore the relationship between sleep parameters and functional outcome

METHODS

Subjects

Recruitment

Hospitalized subjects with moderate or severe TBI were recruited between June 2016 and January 2017 from an intermediate care neuroscience specialty unit in a level-1 trauma center hospital. This 36-bed unit treats adults with acute and chronic neurological /neurosurgical conditions of the brain and spinal cord. Recruitment was limited to this unit because the patient population was representative of the target population. During the months of recruitment, the floor often had a high census (83% of beds occupied by patients).

Screening

Subjects were screened for study eligibility based on the following criteria: 1) Admission diagnosis of blunt TBI confirmed with radiological studies; 2) Glasgow Coma Scale score (GCS) between 3 and 11 on admission to the ED—a score indicative of moderate to severe brain injury (Jennett & Teasdale, 1977); 3) ≥ 18 years of age; 4) having spent <24 hours on the neuroscience unit at time of enrollment; 5) Rancho Los Amigos (RLA) score ≥ 5 to capture subjects able to meaningfully contribute to assessment of rest/activity. Subjects were excluded if they 1) had a pre-existing sleep condition; 2) had a planned length of stay (LOS) of less than 24 hours; 3) or if a legally authorized representative (LAR) could not consent on their behalf.

Sampling

Using consecutive convenience sampling, $N = 17$ subjects were included in the final analysis. The convenience aspects of the sampling process entailed recruiting subjects who were housed on the intermediate-care neuroscience specialty unit. They had to be a patient in this unit in order to be eligible for participation in the study. Potential study subjects were enrolled consecutively as the data collection period rolled on.

Ethical Considerations

Study procedures and forms were explained to subjects. All study procedures took place after approval from the University of Washington's Institutional Review Board (IRB). The subject or their LAR provided written informed consent to participate.

Variables

Subject Characteristics

Subject demographic (age, gender) information was extracted from the EMR and from the trauma registry. Disposition discharge was also recorded from the hospital's trauma registry.

Many of the potential study subjects housed on this unit were transferred from the ICU or from

the emergency department (ED) so they can receive care for their injury. This unit cares for patients whose clinical presentation is stable and does not require emergency department care, yet who are as critically ill to remain under the concentrated surveillance of the ICU.

Injury Variables

Injury characteristics were extracted from the electronic medical record (EMR), the trauma registry, or from direct data collection by the author.

Glasgow Coma Scale (GCS): GCS was used to classify severity of neurological injury (range 3–15). GCS reliability is high ($\alpha=0.85$; Sadaka, Patel, & Lakshmanan, 2012) when utilized in patients with TBI. A higher GCS (14 or 15) indicates the patient is neurologically stable, while a lower GCS (3–6) indicates a deteriorated neurologic state.

Injury Severity Score (ISS): ISS reflects the overall intensity of a subject's injuries (Baker, O'Neil, Haddon & Long, 1974; Baker & O'Neil, 1976) and ranges from 1 (least severe) to 75 (most severe). Higher scores indicate a greater likelihood of mortality (Baker & O'Neil, 1976). The ISS has a high inter-rater reliability ($ICC >0.80$) and a high intra-rater reliability ($\kappa >0.80$; MacKenzie, Shapiro, & Eastham, 1985).

Rancho Los Amigos Scale (RLA): The RLA scale is used to assess a subject's level of cognitive functioning and ranges from 1 to 8. A score of 1 means the subject has no response to external stimuli while a score of 8 means the subject responds purposefully and appropriately. RLA has been shown to have good reliability and validity in the brain injured population (Johnston, Findley, DeLuca, & Katz, 1991). This was measured at study entry.

Functional Independence Measure (FIM®): The FIM is an 18 item scale (13 motor tasks, 5 cognitive tasks) that was used to assess the subject's level of disability at hospital discharge. It has been shown to be sensitive to assessment of patient progress. The FIM includes tasks known

to be affected by sleep including: memory, comprehension, and problem solving. Each item is rated on a scale of 1 to 7 (total range 18-126) with lower scores indicating greater dependence and subsequently greater disability. Construct and predictive validity of the FIM has been demonstrated in TBI patients. Inter-rater reliability of the FIM is reported to be $>.90$ with a $>.90$ test-retest reliability (Hamilton, Laughlin, Fiedler, & Granger, 1994). The author passed the FIM mastery test prior to administration of the measure.

Measurements

Rest/Activity Cycles: Actiwatch Spectrum Plus[®] (Phillips Respironics, Bend, OR, USA) wrist actigraphs were used to obtain assessments on wake bouts, total wake time, and sleep efficiency. The Actiwatch Spectrum Plus is about the size of a standard wristwatch (48mm x 37 mm x 15mm, weighing 31 grams with band) and uses a micro-electro-mechanical systems (MEMS) accelerometer to account for rest/activity cycles (32 Hz sampling rate). White light exposure was measured with photopic illuminance, irradiance, and photon flux capabilities of the Actiwatch Spectrum Plus; white light was used to score actigrams (described later). Actigraphy is a measure of rest/activity cycles and is a reliable and valid alternative for indirect measurement of sleep/wake cycles; the latter of which is gleaned by the gold bar standard of polysomnography (PSG) (Ancoli-Israel et al., 2003). The concordance of actigraphy and PSG has also been demonstrated in patients with TBI (Kamper et al., 2016).

Wake Bouts, Total Wake Time, and Sleep Efficiency: The three sleep parameters of interest--wake bouts, total wake time, and sleep efficiency—were selected because the first two address the intra-sleep concept of “nighttime awakenings” and the third addresses the consolidation of sleep; “nighttime”, in the current study, is defined as the patient-specific interval

known as the “SLEEP interval” in actigraphy recording. By “patient-specific”, I mean to say that each patient has a slightly different duration of nighttime sleep. The details of this distinction are described below under the heading entitled “Scoring”. Nighttime awakenings are a particularly important concept in the hospitalized patient with moderate and severe TBI for two reasons: 1) a hospitalized patient waking from their sleep is a behavior often attributed to *interruptions*. These interruptions typically come from hospital staff and other environmental factors like roommate needs, noise levels and light exposure; 2) patients with a TBI are predisposed to fragmented sleep—a class of sleep deprivation that manifests as a subject being spontaneously awakened from their sleep. A similar concept-- *arousal* has been used interchangeably with awakenings, but is distinctly different in that arousals have a neurophysiologic origin (used to indicate cortical events) and are not always perceived by the subject. Conversely, an awakening is behavioral in origin because in many cases it is readily perceived by the subject and on occasion, the observer.

Wake Bouts: This is a count variable (non-negative integer) and is defined as the total number of wakefulness periods recorded during the subjects sleep period. Wake bouts have been used as a sleep parameter in other studies that have aimed to assess sleep fragmentation with actigraphy (Aubert-Tulkens, Culée, Harmant-Van Rijckevorsel, & Rodenstein, 1987; O’Driscoll, Foster, Davey, Nixon, & Horne, 2010). A higher number of wake bouts indicate a higher number of periods of wakefulness.

Total Wake Time: This is a discrete variable and is defined as the total amount of minutes a subject remains awake during their sleep period. More minutes of total wake time indicates more time a subject is awake when they should be sleeping. Total wake time, like wake bouts, can be used to assess sleep fragmentation (Spriggs, 2015). Total wake time corresponds to

another sleep variable in this current study—sleep efficiency; increased total wake time often results in decreased sleep efficiency (Spriggs, 2015).

Sleep Efficiency: This is a discrete variable and is defined as the percentage of total time a subject actually spent sleeping in their hospital bed. Although sleep efficiency does not differentiate brief occurrences of wakefulness, its purpose is to provide an overall idea of the subjects quality of sleep (Shrivastava, Jung, Saadat, Sirohi, & Crewson, 2014) . A healthy adult with a normal sleep/wake cycle may have 90% sleep efficiency (Spriggs, 2015).

The Actiwatch was set to record rest/activity cycles at 30-second epochs. Only nighttime data were used in the analysis and daytime naps were not assessed. Prior to conducting the research study, the authors considered the use of a sleep diary and the likely reliability of the patient’s account of their sleep behavior; however, they were not used because the author could not ensure high-quality sleep logging would take place, either owing to the relatively low priority of a sleep diary for the nursing staff had they been queried and to subjects generally being poor historians subject due to injury (Nazem, Forster, Brenner, & Matthews, 2016).

Scoring. Phillips Actiware[®] software (version 6.0.9) was used to score the actigraphy data. Exposure to white light was used to score rest intervals in the absence of a sleep diary. This standard scoring algorithm was developed by experienced sleep researchers at the University of Washington Center for Innovation in Sleep Self-Management and has been used in previous studies (Buchanan et al., 2017).

Scored actigrams were digitally transformed into a CSV (.csv) file and then subset to include only “SLEEP” intervals which varied *per* subject and *per* night. As a result, each subject had repeated measures of wake bouts, total wake time, and sleep efficiency for each night of

stay. Night of stay was the recorded number of nights a subject was housed on the unit, an important variable since not all subjects had the same number.

Protocol Design

The current study utilized a single cohort design and sought to assess the feasibility and logistic concerns of conducting an ambulatory sleep study in this target population. Actiwatches were calibrated before each use. The author initially screened potential study subjects using the EMR. Once a potential subject was identified, the author arrived on the unit and verified patient condition with the bedside nurse before approaching the subject/LAR. At time of approach, the RLA assessment was performed to verify eligibility for study participation. If eligible and interested, the subject (or the LAR) was approached to provide informed consent.

Following informed consent, an Actiwatch was placed on the non-dominant wrist of the patient. If the intended wrist was blocked due to presence of an IV, sling, or cast, for example, the watch was placed on the other mobile wrist. The actiwatch collected data for a maximum of 5 consecutive nights or until the subject was discharged (whichever was shorter). At the end of the data collection period, the actiwatch was removed by the author and the data files were uploaded to a secure computer for analysis.

Data Management

The data files of three subjects were not included because they were either yielded insufficient data or corrupted data. There were N= 17 complete data files from the actigraphy watch were used in the final analysis. The “SLEEP” rows of each subject were manually extracted from the digitized actiwatch file and stored in a different csv.file that contained all the “SLEEP” rows from each subject. The data were then read into RStudio software (R version 3.3.1) to be analyzed.

Data Analysis

Descriptive

Bivariate statistics and descriptive statistical analyses were used to describe wake bouts, total wake time, sleep efficiencies, injury variables, functional outcome, and subject demographics. Some subject characteristics were also described using categorical data. For example, a subjects injury was identified in terms of neuro-imaging descriptions, like “SDH with 11mm MLS”. This means that a subject suffered a kind of traumatic brain injury, called a “subdural hematoma” or “SDH” which refers to the anatomical location of the injury. The acronym “11mm MLS” refers to a state of the TBI in which accumulation of volume in the patients cranial vault (skull) has caused the brain’s structures to “shift” from their *normal* midline position to either the left or the right by 11 millimeters. Another example of the categorical data are the subjects destination at discharge (*did the subject go home? Did they go to a skilled nursing facility?*)

Hierarchical Mixed Linear Regression

With RStudio software data were fit using the Linear Mixed-Effects function in the lme4 R package (Bates, Maechler, Bolker, & Walker, 2015). This approach was used to analyze the nested, repeated measures observations (N = 61 nights of observation *over* N = 17 subjects). Although the subjects had various nights of stay, I accounted for the variation for these nights of stay in my statistical analysis. I did this by using a hierarchical mixed linear regression where the relative weights of each subjects measures is determined by both the sample size in the group and the variation of measures within and between groups (Gelman & Hill, 2007). In this way, a subject who had 1 night of data could be evaluated on the same “scale” in the regression model as a subject with 5 nights of data. In sum, the hierarchical mixed linear regression model is a

compromise between two extremes of statistical analysis that would either ignore the variation between the subjects or overstate the variation between subjects (Gelman & Hill, 2007).

Model Selection and Interpretation

A reference model or “null model” was chosen for each sleep parameter (outcome variable) and controlled for age as a confounder (Arnardóttir et al., 2010). A single predictor variable was entered into the null model based on the significance and strength of the Pearson-r correlations. The structure of the model was set up much like a simple linear regression in that only one sleep parameter was assessed with only one predictor variable. As a reminder, the predictor variables are GCS, RLA, ISS, Night of stay, and gender. Each predictor variable was entered into its respective linear mixed effects model as a fixed effect only. The subsequent simple linear mixed effects model was compared to its respective null model using both the Bayesian Information Criterion (BIC) (a lower BIC indicating a better model) and an analysis of variance that tested whether the simple linear mixed effects model significantly differed from the null model.

Multiple Linear Regression

A multiple linear regression was conducted to assess whether the sleep parameters under investigation could reliably predict the subjects’ functional outcome. To do this each subjects respective sleep parameter was aggregated based on its median. Each sleep parameter was then set as a predictor variable and controlled for age; using the sleep variables in this way is different from the previous analyses that were described because they are now the *independent* variable. The FIM score represents the subject’s functional outcome and was set as the outcome variable (dependent variable) in the statistical analysis.

Median values of the sleep parameter were used, as opposed to mean values, because this is a between-person analysis. The reason median value of the sleep parameters were used as opposed to the mean values is because the sample size is smaller ($N = 17$ as opposed to $N = 61$ over $N = 17$ in previously described analysis) and the data are not normally distributed. While this has always been the case for the previously described analysis, varying night of stay become a problem because the number of observations has decreased from 61 to 17.

For clarity, an example of the analysis described would go as follows: the median value of wake bouts for subject 004 was entered into a multiple linear regression model as a predictor variable, age was entered as a confounding variable, and FIM was entered into the model as an outcome variable. This was repeated for subject 004's total wake time and sleep efficiency.

An additional analysis was done to assess whether the sleep parameters for the first night of each subjects stay could reliably predict their functional outcome. This was done by filtering each sleep parameter by the first night only. For example, the first night of subject 004's wake bouts was put into a multiple linear regression containing FIM as the outcome variable, wake bouts as the predictor variable, and age as the confounding variable. This was repeated for 004's total wake time, and for their sleep efficiency.

Significance Levels

Because this was an exploratory study, we took a conservative approach to entering variables in the each of the statistical models described. Variable pairs that had a Pearson- r correlation p -value of ≤ 0.10 were entered into its respective model (hierarchical linear regression model or multiple linear regression model). However, a p -value of 0.05 or less was used to indicate statistical significance.

RESULTS

Feasibility of Measuring Rest-Activity Cycles in Hospitalized TBI Patients

Figure 1 outlines how study subjects were screened and enrolled. Eighty-eight percent ($n = 45/n = 51$) of the subjects screened were eligible. Of those eligible 44% ($n = 20/n = 45$) were enrolled and 13 of the 20 subjects required a LAR. Data from three of the 20 enrolled subjects were not used because 2 subjects had incomplete actigraphy readings and 1 subject, previously thought to be new to the unit, was *returning* to the unit a surgical procedure. Moreover, maintaining open communication with the patient's family, the unit secretaries, charge nurses, the nurse manager and the bedside nurse helped to maintain the integrity of the study protocol. For example, having a physical drop box for the actiwatches in the main nurses' station worked well because managing the watch in the event of a sudden discharge was one less thing for them to plan for.

Participant Characteristics and Injury Variables

The sample consisted of mostly White American males and the average age of the sample was 63.4 years ($SD = 17.9$; See Table 1). The mechanism of injury for a majority of the sample ($n = 10$) was by falling. Neuroimaging results show that most of the sample also suffered subdural hematomas. Of the 17 subjects, eight had mid-line shift. The sample's emergency department (ED) GCS scores reflected moderate and severe TBI ($M = 8.8, SD=4.9$) and at enrollment, mean RLA score was 7.6 ($SD = 0.85$). Both of these are congruent with eligibility criteria.

Sample ISS of about 23 ($SD = 6.7$) and 8 of 17 subjects (47%) were discharged to home, while 35% were discharged to a skilled nursing facility (see Table 1 for further details). The

average FIM at discharge was 48 ($SD = 14.5$) indicating severe disability (Sandhaug, Andelic, Vatne, Seiler, & Mygland, 2010).

Description of Sleep Parameters & Graphical Reproductions

Across the sample, there was a total of 61 nights of observation and the average number of nights of stay was 2.6 ($SD = 1.3$). To get the sample average of wake bouts, total wake time, and sleep efficiency, the median number of each sleep parameter was found for each subject's hospital stay, and the resulting 17 values were averaged. Therefore, the average number of wake bouts of the sample was 41, the average total wake time was 74 minutes (about 1 hour and 14 minutes), and the average sleep efficiency was 73%.

Figure 2 shows side-by-side graphical reproductions (actograms) of two subjects: one with the best sleep efficiency (Subject 4; 93%), the other with the worst (38%). There is a cyclical decrease and increase in movement and light for subject 4. This is evidence of a regular rest and wake activity, respectively. Conversely, the light/movement activity for subject 014 is not consolidated and has with frequent wake bouts.

Relationships: Injury Variables and Sleep Parameters

There was a moderate, positive correlation between RLA score at baseline and each of the 61 nights of recorded wake bouts ($r = 0.37$, $p\text{-value} = 0.004$; see Table 2). Though not statistically significant, there was a positive relationship between GCS and wake bouts ($r = 0.23$, $p\text{-value} = 0.07$) and negative relationship between ISS and wake bouts ($r = -0.25$, $p\text{-value} = 0.06$). There was a statistically significant negative relationship between GCS ($r = -0.31$, $p\text{-value} = 0.01$) and RLA ($r = -0.29$, $p\text{-value} = 0.02$). There was also a statistically significant positive relationship between sleep efficiency and gender ($r = 0.30$, $p\text{-value} = 0.02$). Finally, for total

wake time, there were statistically positive relationship with GCS ($r = 0.39$, $p\text{-value} = 0.002$) and then with RLA ($r = 0.32$, $p\text{-value} = 0.01$).

Each of the above pairs were entered as fixed effects into the multi-level linear regression model and controlled for age. Only RLA was shown to be a statistically significant predictor of the number of wake bouts ($\chi^2(1) = 4.44$, $p = 0.04$). Aside from RLA and wake bouts, and despite significant correlations, there were no other statistically significant relationships between other injury variables (GCS, ISS) and other sleep variables (see Table 3).

Sleep Parameters and Functional Outcome

The Pearson- r correlation matrix (see Table 4), does not indicate any p -values less than 0.10 and no p -values less than 0.05 for each of the measured sleep parameters and FIM. The relationship between FIM and wake bouts was very weak in strength ($r = 0.06$, $p\text{-value} = 0.82$) while FIM and sleep efficiency had a moderate, negative relationship ($r = -0.33$, $p\text{-value} = 0.18$). There was no relationship between FIM and total wake time ($r = 0.00$, $p\text{-value} = 0.98$).

As mentioned before, sleep parameters from night 1 and FIM were also entered into a multiple linear regression that controlled for age. However, the results are not presented here because the results are not significant.

DISCUSSION

The current study shows that it is feasible to study sleep and wake patterns in this patient population despite the abbreviated hospitalization period. This is consistent with Chiu et al (2013) and Duclos, Dumont, Blais et al. (2014) since they also conducted actigraphy assessments on patient with TBI who were hospitalized. Like Chiu et al. (2013), the current study focused exclusively on patients with moderate or severe TBI that were housed on an intermediate care neuroscience specialty unit. In effect, the current study was confirmatory. However, it makes a

unique contribution in the way of examining the how poor sleep affects the functional outcome of a patient with moderate and severe TBI *during* the acute (yet non-ICU) phase of hospitalization. Relative to normative levels of wake bouts, total wake time, and sleep efficiency (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004; Shrivastava et al., 2014), the sleep behavior in the present sample is consistent with that of others noting pathological sleep following TBI (Grima, Ponsford, St Hilaire, Mansfield, & Rajaratnam, 2016; Parcell et al., 2006; Ponsford & Sinclair, 2014; Wiseman-Hakes et al., 2016). Specifically, poor consolidation of sleep as evidence by the low levels of sleep efficiency, high wake bouts, and longer time spent awake in periods where the patient should be sleeping.

Relationship between Rancho Los Amigo and Wake Bouts

In the present report, we found that RLA was correlated with wake bouts. This is closely related to research findings from Duclos et al. (2017) which noted RLA to be significantly correlated with nighttime sleep fragmentation among acute (during ICU stay and after ICU stay) patients with TBI. Chiu et al. (2014) show similar findings in their study that assessed cognitive recovery with RLA; however, they found that RLA was only significant mediator of sleep during the patient's *daytime* sleep period.

Effectively, the significance of RLA and wake bouts in the current study suggest an important point about sleep disturbance in hospitalized patients with TBI. That is, those who have a higher level of cognitive functioning appear to have a greater sensitivity to awakenings. Put another way, these patients seem to have a lower threshold to being awakened from their sleep. For clinicians, this means that patients who demonstrate more awareness upon clinical assessment (perhaps their eyes track, they can follow commands most of the time) could benefit from bundled care and multi-modal interventions that decrease likelihood of awakenings (private

rooms, placement that is not near a door that constantly opens and closes, for example). This is important because, despite the fact that these patients have moderate and severe TBI, the evidence in the current study (and that from other studies) suggests that their sleep can still be impacted if they have increased levels of cognitive functioning. These levels, ironically, are likely lower than patients with a mild TBI or who have no TBI at all. Additionally, it may also be the case that actigraphy may not be sensitive enough to capture disturbances to sleep that may be taking place. Perhaps other methods of sleep pattern evaluation like PSG or EEG, which capture the brain's neuro-stimulation, may show that disturbances to sleep are inevitable and persistent among patients housed in this phase of hospitalization.

However, a study, perhaps with a control group needs to be conducted to further investigate this. Moreover this is a nuanced finding that corresponds with the sometimes unique and nuanced clinical presentation of patients with moderate TBI like many of the subjects in this current study (Lund et al., 2016).

No Relationship between Other Injury Variables and Sleep Parameters

It was surprising that none of the other injury-related variables correlated with any of the other sleep parameters. Especially since there is evidence that shows poor sleep is both a common symptom of TBI (Grima, Ponsford, Rajaratnam, Mansfield, & Pase, 2016) and that poor sleep can undermine rehabilitative efforts (Mazwi, Fusco, & Zafonte, 2015). In addition to the small sample size, another reason for this finding may be that the evaluative structure of the injury variables was too global in scope and not reflective of the sample's *true* clinical disposition with regard to sleep. Perhaps there was not enough variation in the sample's injury variables to detect their contributions to sleep.

No Relationship between Sleep Parameters and Functional outcome

Several studies, including systematic reviews and original research, have shown a relationship between sleep and functional outcome (Evans & Bartlett, 1995; Mahmood, Rapport, Hanks, & Fichtenberg, 2004; Ouellet, Beaulieu-Bonneau, & Morin, 2015b; Sandhaug et al., 2010; Sandsmark et al., 2016). However the results of the current study show otherwise. Evans et al (1995) and Sandsmark et al (2016) are the two few studies that objectively (cEEG) assessed sleep in relation to a functional outcome among patients with moderate and severe TBI. Sandsmarks et al.(2016) measured sleep using cEEG and identified a study subject as having good sleep architecture if they had K complexes, sleep spindles, and vertex waves; the results of their study showed that subjects who had sleep features (compared to subject who did not), were more likely to have a higher modified Rankin Scale score (mRS). Like FIM, the mRS measures the degree of a person's disability when they carry-out their daily activities of living; it is a common measure used in stroke patients. Sandmarks et al. 2016 also found that sleep elements detected on cEEG was a reliable predictor of the subjects functional outcome independent of the subjects GCS on admission. A similar result was found in the Evans et al. (1995).

Moreover, driving independently and working for pay were two aspects of long term functional outcome following TBI in other studies (Schwab et al., 2015) and perhaps development of an acute care counterpart to those outcome measures may be an important point of investigation in future studies. Although systolic blood pressure, brainstem injury, and Glasgow coma outcome scale were shown to be reliable predictors in older adults with moderate and severe brain injury (Utomo, Gabbe, Simpson, & Cameron, 2009), their outcomes (in-hospital mortality and at 6 months post injury) were different from functional outcome which was the outcome in the current study.

Limitations

The feasibility design of this study did not allow for a larger sample size, which provided limited power for the analysis. However, the within-person analyses may have somewhat mitigated this concern. Perhaps more frequent measures of injury variables and functional outcome variables should have been taken. For example, a GCS score should have been taken not only at admission to the hospital, but at various phases during hospitalization. The same would apply for functional outcome assessments. Doing this could have shown the *trajectory* of a subject's clinical presentation and may have provided variation in the sample's injury and functional outcome variables.

The current study also focused solely on nighttime sleep and perhaps incorporating daytime sleep may have been useful to establishing a relationship between sleep parameters and injury variables (Chiu et al. 2014). However, the difficulty in assessing when the subject goes to sleep and wakes from sleep is a methodological challenge because one cannot pinpoint when these behaviors occur without incorporating a participant-observation component. Also, this behavior cannot be determined based solely on actigraphic assessment.

CONCLUSION

This study adds to the growing body of literature about sleep disturbances among people with TBI by focusing on characteristics of patients with moderate and severe injury who are hospitalized in an intermediate care neuroscience unit. While studies with more participants and with slightly different measures of assessment of disability are needed to show the nature of relationship between injury variables and sleep parameters, the current study shows the relative feasibility of accessing the patient population to do so. Furthermore, the study findings correspond with other research about the impact of TBI on sleep. Stakeholders in hospital care

and management should know that patient with TBI are prone to disturbed nighttime sleep *during* their hospitalization; in turn, these disturbances increase as cognitive status improves.

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Tables

Table 3.1. Demographic and Clinical Characteristics of Subjects

ID	Age	Sex	Mechanism of Injury	GCS	ISS	RLA	FIM	Neuroimaging Results	Nights of Stay on Unit	Discharge Destination	Median Total Wake Time (min.) across nights	Median Wake bouts (counts.) across nights	Median Sleep Efficiency (%) across nights
2	34	M	Assault	7	29	7	50	(R) EDH, 6mm MLS	1	Home	109	37	64
3	68	F	Fall	3	16	8	52	(L) SDH, 4mm MLS	5	SNF	34	33	87
4	58	M	Hit by car	3		5	20	Diffuse (L) SAH, 8mm MLS	5	SNF	16	17	93
6	30	M	Sporting Accident	12	26	8	59	Large (B/L) frontal IPH, Small Anterior-Temporal IPH, vasogenic edema Persistent IPH of (R) cerebellum, SAH of (B/L) frontal and anterior temporal lobe	2	Rehab	53	22	67
7	38	M	Sporting Accident	3	35	7	51		5	Home	50	29	66
8	70	M	Fall	12	26	8	54	(L), SDH, 4mm MLS	5	SNF	50	30	86
9	50	M	Fall	3	26	8	32	(R) SDH, 10mm MLS	5	Rehab	58	42	84
10	77	M	Fall	3	14	8	38	(L) SAH, petechial parenchymal hemorrhage, facial fx Small volume traumatic (B/L) SAH, occipital and (R) parietal Subgaleal hemorrhage	3	Home	88	62	88
11	27	M	Hit by car	13	13	8	64	Small (R) temporal SDH, pneumocephalus and basifrontal hemorrhagic contusions	2	Home	106	70	86
12	35	M	Sporting Accident	13	18	8	78		3	Home	16	9	45
14	75	M	MVA	14	22	8	56	Diffuse scattered SAH, IVH	5	Rehab	212	66	38
15	78	F	Fall	14	27	8	58	(B/L) SDH, (R)-to-(L) MLS	5	Home	106	68	84
16	79	M	Fall	13	16	8	58	(L) SDH, 12mm MLS	5	SNF	77	46	67
17	70	M	Fall	3	25	7	40	Large (R) SDH, 2cm MLS, (L) side hydrocephalus	1	Home	86	51	70
18	79	F	Fall	9	25	8	54	Large (L) SDH, 3mm (R)-to-(L) MLS	4	SNF	70	38	80
19	83	M	Fall	13	25	8	28	(L) SDH, 11mm MLS, (L) Uncal herniation	4	SNF	101	30	57
20	85	M	Fall	14	9	8	65	(R) frontotemporal SDH, mild vasogenic edema	1	Home	34	41	78
Summaries	(M = 63.4, SD = 17.9)	M/F 14/3	1 Assault; 1 MVA; 3 Sports Related; 2 Hit by car; 10 Falls	(M = 8.8, SD = 4.9)	(M = 23.6, SD = 6.7)	(M = 7.6, SD = 0.9)	(M = 48, SD = 14.5)	1 EDH; 1 IPH; 3 SAH; 2 Combination injuries; 10 SDH	(M = 2.6, SD = 1.3)	3 rehab; 8 Home; 6 SNF	(M = 74, SD = 47)	(M = 41, SD = 18)	(M = 73, SD = 16)

Abbreviations: MVA, motor-vehicular accident; GCS, Glasgow Coma Scale; ISS, injury severity scale; RLA, Rancho Los Amigo; FIM, Functional Independence Measure; MLS, midline shift; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage; IPH, intraparenchymal hemorrhage; EDH, epidural hemorrhage; (B/L), bilateral; (L), left; (R), right

Table 3.2. Pearson – r correlation matrix of Injury Variables and Sleep Parameters, Within-Person Analysis (Multi-Level Model)

	Night	WB	Sleep Eff.	TWT	AGE	GCS	RLA	ISS	Gender
Night	1								
WB	-0.11	1							
Sleep Eff.	-0.05	0.01**	1						
TWT	-0.07	0.71	-0.45**	1					
Age	0.12	0.18	0.12	0.17	1				
GCS	-0.05	0.23*	-0.31**	0.39**	0.31**	1			
RLA	-0.06	0.37**	-0.29**	0.32**	0.19	0.49**	1		
ISS	0.15	-0.25*	-0.04	-0.09	-0.27**	-0.29**	-0.46**	1	
Gender	0.09	0.12	0.30**	-0.10	0.35**	-0.01	0.23*	-0.09	1

Note. * indicates p-value of ≤ 0.10 , ** indicates p-value of ≤ 0.05

Table 3.3. Model Selection and corresponding Bayesian Inference Criterion (BIC) value

Model	BIC
<i>Base model: TWT ~ Age + (1 Subject)</i>	661.4
Base model + GCS	663.3
Base model + ISS	665.5
Base model + RLA	663.7
<i>Base model: WB ~ Age + (1 Subject)</i>	554.8
Base model + GCS	557.9
Base model + ISS	556.9
Base model + RLA	554.5
<i>Base model: Sleep Eff. ~ Age + (1 Subject)</i>	521.7
Base model + GCS	523.3
Base model + ISS	525.7
Base model + RLA	524
Base model + Gender	524.3
Tests of Significance with Analysis of Variance (ANOVA)	Significance Test
<i>Model Pair (Base model, Test model)</i>	χ^2 (df) = chi-square value, p-value
(Base model: TWT ~ Age + (1 Subject), Base model + GCS)	χ^2 (1) = 2.24, p = 0.13
(Base model, Base model + ISS)	χ^2 (1) = 0.001, p = 0.98
(Base model, Base model + RLA)	χ^2 (1) = 1.75, p = 0.19
(Base model: WB ~ Age + (1 Subject), Base model + GCS)	χ^2 (1) = 0.99, p = 0.33
(Base model, Base model + ISS)	χ^2 (1) = 2.02, p = 0.16
(Base model, Base model + RLA)	χ^2 (1) = 4.44, p = 0.04
(Base model: Sleep Eff. ~ Age + (1 Subject), Base model + GCS)	χ^2 (1) = 2.6, p = 0.11
(Base model, Base model + ISS)	χ^2 (1) = 0.11, p = 0.73
(Base model, Base model + RLA)	χ^2 (1) = 1.8, p = 0.17
(Base model, Base model + Gender)	χ^2 (1) = 1.5, p = 0.22
Abbreviations: GCS, Glasgow Coma Scale; ISS, injury severity scale; RLA, Rancho Los Amigo; FIM, Functional Independence Measure; BIC, Bayesian Inference Criterion; TWT, total wake time; WB , wake bouts; Sleep Eff., sleep efficiency; df, degrees of freedom.	

Table 3.4. Pearson – r correlation matrix of study variables, *Aggregated by Median of Sleep Parameters: Functional Independence Measure Analysis*

	Night	WB	Sleep Eff.	TWT	FIM	Age	Sex
Night	1						
WB	-0.06	1					
Sleep Eff.	0.10	0.14	1				
TWT	0.02	0.72**	-0.43*	1			
FIM	-0.24	0.06	-0.33	0.00	1		
Age	0.28	0.29	0.11	0.19	-0.23	1	
Sex	0.32	0.15	0.32	-0.05	0.14	0.32	1

Note. * indicates p-value of ≤ 0.10 , ** indicates p-value of ≤ 0.05

Figures

Figure 1. Flow Chart of Recruitment

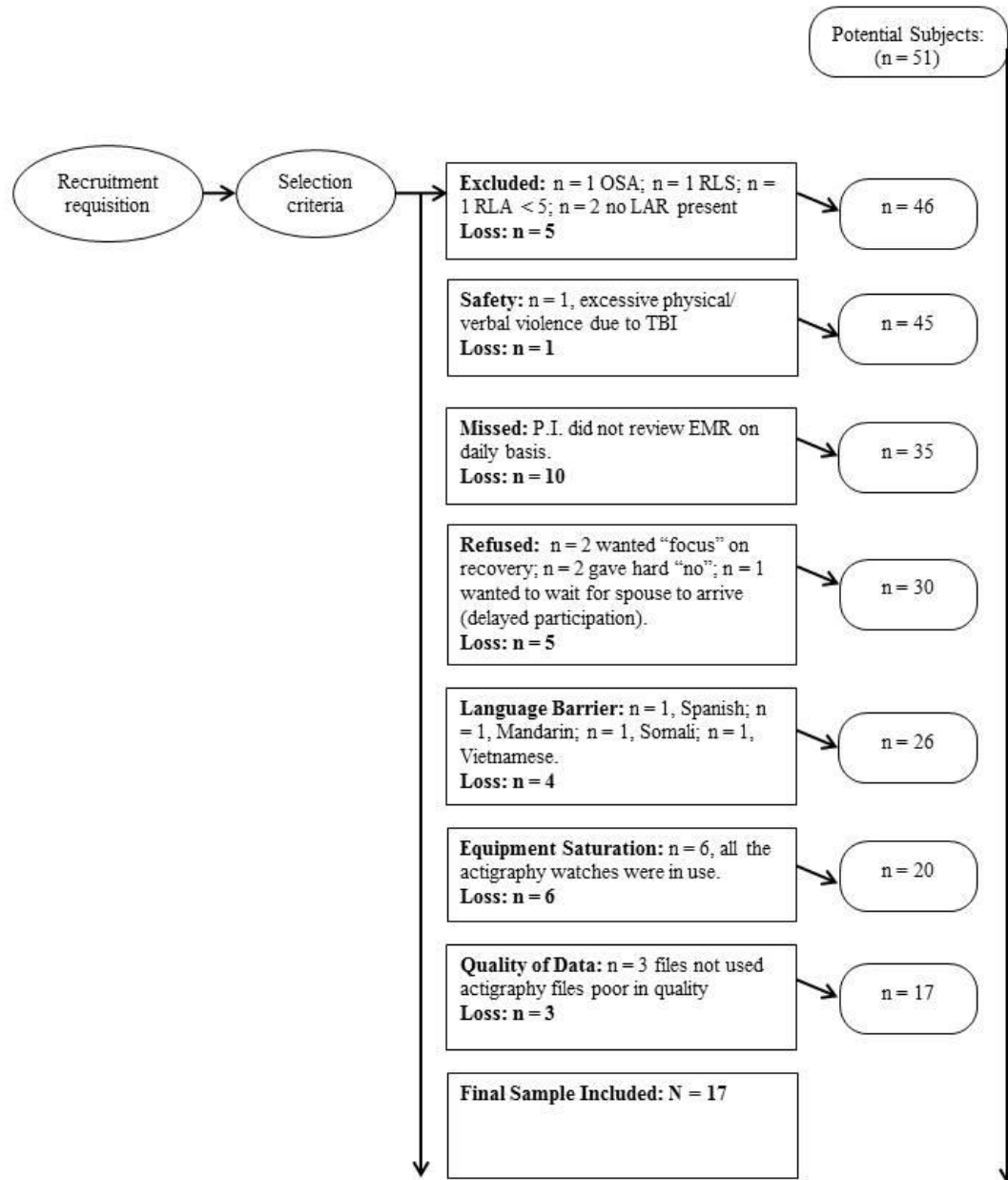
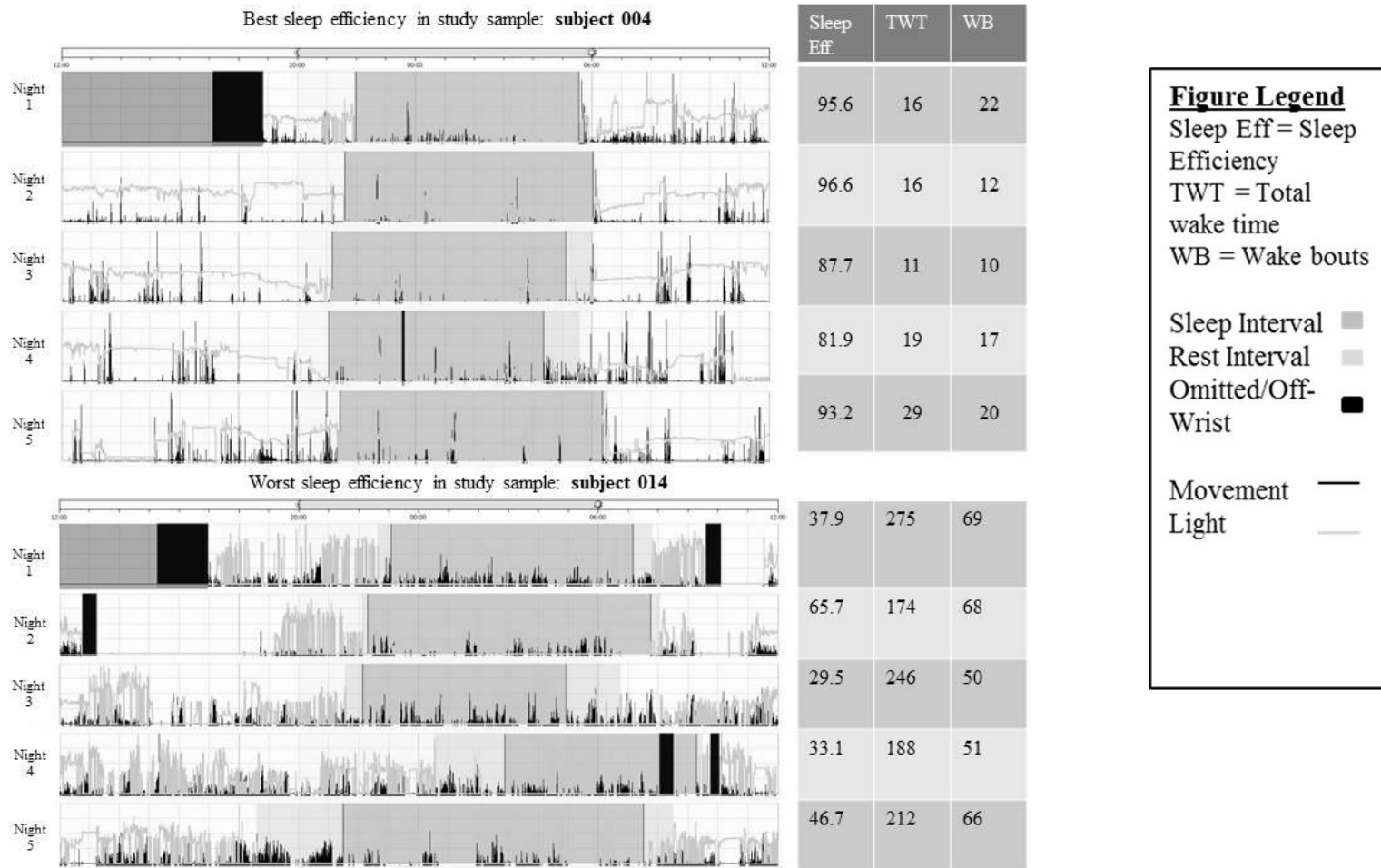


Figure 2. Comparison of best and worst sleep efficiencies in the study sample



CHAPTER 4

Predictors of Nighttime Awakening on a Neuroscience Specialty Unit: Ambient Environmental Stimuli and the Patient with Moderate-to-Severe TBI

Abstract

BACKGROUND: Little is known about the nighttime awakenings of hospitalized patients with moderate and severe traumatic brain injury (TBI) on neuroscience care units. Although several studies have demonstrated poor sleep architecture among the hospitalized population of patients with TBI, it is still unclear what role the ambient environment plays.

OBJECTIVE: The purpose of this pilot study was to examine the exposure pattern of ambient stimuli and its influence on the nighttime awakenings of patients with moderate to severe TBI. **AIMS:** 1) Describe the individual and cumulative influence of sound, light, and movement on the probability of nighttime awakenings of subjects housed on an intermediate neuroscience specialty unit following moderate to severe TBI. 2) Describe the association between ambient stimuli and the length of the subject's night of stay on the unit.

METHODS: Subjects were recruited from a neuroscience unit in a level-1 trauma center in Washington State. A custom multi-sensor that logged sound [dB(A)], light (lux), and passive infrared motion (p) sampled the patient's room environment at one-second epochs. A wrist worn Actiwatch Spectrum Plus actigraph concurrently sampled the patient's rest-wake activity at 30-second epochs. At the end of the five-day study period, data from both instruments were merged. In order to assess the probability of the subject being awakened from sleep by

environmental stimuli detected by the sensor, nighttime data (between 2000 hours and 0800 hours) were analyzed using bivariate statistics and multi-level hierarchical logistic regression.

RESULTS: The sample was predominantly white, non-Hispanic, and male (n=18). The average age of subjects was 65 years, and the average admission Glasgow Coma Scale score was 9. Mean sound, light, and movement during nighttime hours were 52dB(A), 9 lux, and 0.28 (p), respectively. With each stimuli set at its average, there is a 20% probability that a patient will awaken from their nighttime sleep. The probability of a patient being awakened from their sleep decreases to 15% (statistically significant) when movement is set at 0 (p). Movement in the room and sound were significant predictors of nighttime awakenings, while light was not. **DISCUSSION:** As a consideration, future studies should examine the source of these environmental stimuli with either a participant-observer component or with video for which “critical events” of sensor triggers can be documented.

Key words: Ambient, traumatic brain injury, environment of care, sensor

INTRODUCTION

Recent statistics from the Centers for Disease Control (CDC) indicate that nearly 300,000 people were hospitalized for traumatic brain injury (TBI) in 2013 (Taylor, Bell, Breiding, & Xu, 2017). Uninterrupted sleep, while essential for recovery after TBI (Ouellet et al., 2015b; Ponsford & Sinclair, 2014), is not always attainable in a busy hospital setting because patients are constantly monitored and surveilled (Yoder, Yuen, Churpek, Arora, & Edelson, 2013b). While housed in the intermediate care unit (the phase of hospitalization that follows intensive care), patients with TBI may experience sleep problems brought on by their injuries and by the care environment itself (McNett, Sarver, & Wilczewski, 2012). This paper explored the relationship between nighttime awakenings and the pattern of ambient stimuli exposure in the hospital rooms of patients with moderate and severe TBI. This is important because uncovering mutable causes of nighttime interruptions can assist with development of nursing-based sleep hygiene interventions for these patients. The stimuli of interest are sound level, light intensity, and the movement of others (primarily provision of care by nursing staff).

BACKGROUND

Neuroscience units are often the setting where patients with moderate and severe TBI begin their recovery process. However, it is not clear how the intermediate care neuroscience unit setting may influence the sleep that is necessary for these patients' optimal health and well-being. Also unclear is the extent to which specific ambient stimuli like sound, light, and movement contribute to disturbed sleep.

Of the few studies that have objectively explored aspects related to nighttime awakenings among hospitalized patients with TBI, two were based in the intensive care unit (Duclos et al., 2014; Wiseman-Hakes et al., 2016). The other two involved patients housed on wards (Chiu et

al., 2013b, 2014), but neither evaluated the contribution of the ambient environment to sleep. Results from all four of these studies demonstrate that patients with TBI experience poor sleep consolidation (Chiu et al., 2013; Chiu et al., 2014; Duclos et al., 2014) and poor sleep architecture [Wiseman- Hakes et al., 2016, which used polysomnography (PSG)]. Nevertheless, the hospital environment has been a noted cause of sleep disturbance, not only due to patient care delivery by hospital staff (Fanfulla et al., 2011b; Uğraş, Babayigit, Tosun, Aksoy, & Turan, 2015), but also because of noise and light exposure (Gathecha et al., 2016; Thomas et al., 2012). As noise, light, and motion are factors that can be targeted for change if there is an association between these stimuli and nighttime awakenings in TBI patients, there is a need to investigate this gap in knowledge. Measurement of such stimuli by direct observation could worsen rest/activity patterns due to intrusiveness. However, innovative methods such as sensor technologies have the potential to overcome this obstacle in order to develop a “profile” of ambient stimuli exposure in the neuroscience unit and inform patient-level and unit-level interventions (Kartakis, Sakkalis, Turlakis, Zacharioudakis, & Stephanidis, 2012; Patel, Park, Bonato, Chan, & Rodgers, 2012). Using objective measurement allows for a more reliable correlation between patients sleep patterns and *actual* rather than *perceived* ambient conditions.

PURPOSE

The purpose of this pilot study was to examine the exposure pattern of ambient stimuli and its influence on the nighttime awakenings of patients with moderate to severe TBI.

AIMS

- *Aim 1:* Describe the individual and cumulative influence of sound, light, and movement on the probability of nighttime awakenings of subjects housed on an intermediate neuroscience specialty unit following moderate to severe TBI.

- *Aim 2:* Describe the association between ambient stimuli and the length of the subject's night of stay on the unit.

METHODS

Subjects

Recruitment & Screening

Between June 2016 and January 2017, hospitalized subjects with moderate or severe TBI were recruited from the neuroscience unit of a level-1 trauma center. The 36-bed unit treats adult patients with acute and chronic neurological/neurosurgical conditions and injuries to the brain and spinal cord.

The following inclusion criteria were used to screen eligible subjects: 1) Admission diagnosis of blunt TBI confirmed with radiological studies; 2) Glasgow Coma Scale score (GCS) between 3 and 11 on admission to the emergency department (ED)—a score indicative of moderate to severe brain injury (Jenett & Teasdale, 1977); 3) ≥ 18 years of age; 4) having spent <24 hours on the neuroscience unit at time of enrollment; 5) Rancho Los Amigos (RLA) Cognitive Functioning Scale score ≥ 5 to capture subjects with sufficient cognitive capability to be able to meaningfully contribute to assessment of rest/activity. Subjects were excluded if they 1) had a diagnosed, pre-existing sleep condition, or 2) had a planned length of stay (LOS) of less than 24 hours. Institutional Review Board (IRB) approval was obtained from the University of Washington for all procedures. Subjects or their legally authorized representative (LAR) provided written consent to participate. Using purposive, consecutive sampling, 20 patients were enrolled in the study.

Variables

Multi-Sensor: A custom-made electronically-powered multisensor device (dimensions 14 x 14 x 8.5 cm) was developed to capture and log the ambient stimuli (sound, light, and motion) for the current study. Developers Ellita T. Williams and Daniel Rowland used material and code primarily provided by AdaFruit[®]. Data were locally collected on an 8 GB SanDisk card. The validation of each component of the sensor was completed prior to deployment in the study as follows:

Sound: The sound pressure capability of the multisensor was integrated from a sound level meter. The settings were “A” and “slow,” weighted. “A”-weighting refers to the noise weighting filter that closely aligns with the relative loudness that is perceived by the human ear. It was important to set the sound component of this weighting filter because we wanted to capture sound pressure levels that would most likely be perceived by human beings. Likewise, “slow” refers to the relative speed with which human being beings perceive sound pressure. With an accuracy of +/- 2 dB, the range of the sound pressure capability was ~ 40–140 dB. Side-by-side laboratory and clinical reliability and validity testing with a 3M NoisePro Dosimeter (the gold standard) were conducted and results yielded a high level of agreement ($R^2 = 0.99$). Frequency analyses were also conducted with a 3M octave band analyzer to document the frequency range of the neuroscience unit. Results for the noise validation and reliability studies of the sensor have been reported elsewhere (Williams, Cohen, & Thompson, 2016).

Light: Side-by-side laboratory reliability and validity testing between the sensor’s light component and the Digi-Sense[®] (the gold standard) resulted in a high level of agreement ($R^2 = 0.90$). Measured in lumens, the range of the sensor’s light component was between “N/A” (coded as “0”) and 38,966 kilo lux.

Movement: Studies were conducted to determine whether the sensor's motion component activated when someone in front of it. Because passive infrared (PIR) is the underlying technology behind the movement component of the sensor, only human beings would trigger the movement sensor. This is an important concept because inanimate objects would also trigger the movement component of the multi-sensor if a detection method other than PIR was utilized.

Visual inspection of the real-time output was sufficient for this aspect of the sensor. This level of assessment is justified by the principles of construct validity. These motion studies were also conducted in a controlled lab setting in which a human stand-in moved sequentially from left to right and right to left on an equidistant floor grid. It recorded all of the movements made by the test subject.

Measurements

Ambient environment: The ambient stimuli comprise three individual variables: sound pressure (in decibels), light (lumens), and movement (passive infrared signaling). Movement is a binary variable (0 = no movement, 1 = movement). While sound pressure levels and light intensities are continuous variables. Ambient exposure was sampled every second; output was saved to the scan disk as a plain text (.txt) file.

Rest/Activity Cycles: Actiwatch Spectrum Plus[®] (Phillips Respironics, Bend, OR, USA) wrist actigraphs were used to assess the rest/activity cycles from which we would eventually glean the probability of nighttime awakenings. "Rest/activity" is commonly used in the sleep literature to make others aware that the sleep assessment was done with actigraphy. Conversely, "sleep/wake" cycles would suggest that method used in the sleep assessment was conducted by neuro-stimulations studies (polysomnography, electroencephalography).

About the size of a standard wristwatch (48mm x 37 mm x 15mm, weighing 31 grams with band) and showing time of day per military or 24-hour time, this actigraph uses a micro-electro-mechanical systems (MEMS) accelerometer to account for rest/activity cycles (32 Hz sampling rate). The Actiwatch Spectrum Plus measures white light exposure with photopic illuminance, irradiance, and photon flux. Although PSG is the gold standard for assessing sleep-wake patterns and sleep architecture, actigraphy, which measures rest/activity cycles, is a reliable and valid option for indirect measurement in place of PSG (Israel-Ancoli et al., 2003).

The primary variable of interest, nighttime awakenings, is binary, where 0 = sleeping and 1 = awake. The Actiwatch was set to record rest/activity cycles at 30-second epochs. Although day and night data were collected, only nighttime data were used in the analysis. Prior to conducting the research study, the authors considered the use of a sleep diary and the likely reliability of the patient's account of their sleep behavior. Sleep diaries were not used in the present study because the researcher could not ensure high-quality sleep logging would take place, either owing to the subject's poor historicity due to injury or the relatively low priority of a sleep diary for the nursing staff.

Scoring. Phillips Actiware[®] software (version 6.0.9) was used to score the actigraphy data. The beginning and the end of the rest interval were manually entered standard scoring algorithm that was developed by experienced sleep researchers at the University of Washington Center for Innovation in Sleep Self-Management and has been used in previous studies (Buchanan et al., 2017). Given the absence of a sleep diary to indicate initiation of rest and activity intervals, only the parts of the algorithm applying to logged light and activity levels were used.

The actograms were digitally transformed into a CSV (.csv) file and then subset to include only "REST" and "REST-S" data from the period between 2000 hours and 0800 hours; this standard

sleep interval was set based on 1) the absence of a sleep diary, and 2) visual inspection that revealed that most patients were sleeping during these hours.

Night of Stay

This is defined as the number of nights a subject wears the actiwatch and the number of nights a patient is monitored with the multi-sensor. If a subject has on the actiwatch and is monitored with the multi-sensor for five consecutive nights, that subject will have five nights of stay; conversely, if a subject has on the actiwatch and is monitored with the multi-sensor for 1 night, that subject will have the number “1” listed under the variable “nights of stay”. Night of stay on the unit is important because it indicates: 1) how many nights the subject has been enrolled in the study and; 2) it also lends a measure of *how long* the subject has been housed on the unit. Both of these points are important because more nights on the unit could be indirect indicator of how acutely ill the subject is. For the purposes of this study, more nights of stay may also indicate that the subjects’ rest/activity patterns have become more acclimated to the patterns of ambient stimuli exposure.

Injury Variables

Demographic and injury characteristics were extracted from the electronic medical record (EMR) or the trauma registry. GCS score of level-of-consciousness upon ED admission was used to gauge intensity of neurological injury (range 3–15). GCS reliability is high ($\alpha = 0.85$; Sadaka, Patel, & Lakshmanan, 2012) when utilized in patients with TBI. A higher GCS (14 or 15) indicates the patient is stable, while a lower GCS (3–6) indicates a deteriorated neurologic state. The injury severity score (ISS) reflected the overall intensity of a subject’s injuries (Baker, O’Neil, Haddon & Long, 1974; Baker & O’Neil, 1976) and ranges from 1 (least severe) to 75 (most severe). Higher scores indicate a greater likelihood of mortality (Baker & O’Neil, 1976).

The ISS has a high inter-rater reliability (ICC >0.80) and a high intra-rater reliability ($\kappa = >0.80$; MacKenzie, Shapiro, & Eastham, 1985).

Protocol Design

This pilot study utilized a single cohort design. Instruments (sensors and actigraph watches) were calibrated before each use. Prior to approaching the subject and LAR for study participation, the assigned bedside nurse was asked about the subject's condition, as measured by the RLA score, to determine eligibility. Following informed consent, an Actiwatch was placed on the non-dominant wrist of the patient; if this was untenable (due to IV, slings, casts, etc.), then it was placed on the other wrist. The custom multi-sensor device was also installed at this time and was secured to an empty space on the wall adjacent to the head of the subject's bed. Both the Actiwatch and the multisensory collected data for a maximum of five consecutive nights or, if the length of stay was less than five nights, until the subject was discharged. At the end of the data collection period, data files from both the Actiwatch and the sensor device were uploaded to a secure computer in preparation for final analyses.

Data Management

Using RStudio (R version 3.3.1) software, complete data files from both the actigraphy watch and the sensor were joined so the time stamps for both devices were aligned with each other. This was done in two phases: in the first phase, there was joining within each subject since one subject had hundreds of observations; the second phase of joining occurred across each subject so that there was single data frame that contained all of the observations from all of the subjects.

Merging Actigraphy Data and Multisensor Data

To match the sampling interval of the actigraphy data, sensor data were disaggregated from 1-second epochs to 30-second epochs based on maximum values; this means that *maximum* value of sound, light, and motion within the 30-second epoch was extracted and yielded a new value for each 30-second observation. The maximum was chosen over the mean because the authors believed it would better reflect the ambient spikes known to cause interruptions during the nighttime hours. Duplicate values from the sensor were removed and light values that read “N/A” were coded to “0” as this is the sensor's way of indicating that light levels were below the lower limit of detection.

The two sets of data were further matched such that the data file with the smaller number of entries was used as the “base-file.” For example, if there were 3,500 observations in the actigraphy file, but only 3,200 observations in the multi-sensor file, the latter would be used as the “base-file” and the former would be cut by 300 observations to match the multi-sensor file. The result was a merged file that was matched on the basis of time stamps and on the basis of observations.

Visual inspection of plots from the actigraphy and the multi-sensor showed that there was no apparent time lag between the two devices. The merged data files were then filtered to include only observations from 2000 hours to 0800 hours. A “Night” was therefore considered to start at 2000 hours on, for example, 6/27/2016, and end on 0800 hours on 6/28/2016. Daytime naps, meaning actigraphy intervals other than “REST” and “REST-S”, were not included in the analysis of data.

Data Analysis

Descriptive

Descriptive statistical analyses were used to describe ambient stimuli exposure so that means and standard deviations about each stimulus could be reported. This was also the case for nighttime awakenings because it was important to report the overall probability of nighttime awakenings for the sample. Night of stay, a concept defined earlier, was important to report with descriptive statistics since it would yield the average number of nights the subjects in the sample were monitored. Descriptive statistics about injury variable were necessary to indicate the intensity of TBI in this sample. Demographic variables were important to describe with descriptive statistics because they would contextualize, for the reader, what demographic of hospitalized patient was enrolled into the study. Multivariate statistics were used to analyze nighttime awakenings, night of stay, and each ambient stimulus subject demographics because the researcher wanted to understand the association of these variables using correlations and regressions.

Hierarchical Mixed Logistic Regression

With RStudio software (R version 3.2.2; R Core Team, 2015), data were fit using the Generalized Linear Mixed-Effects function in the lme4 R package (Bates, Maechler, Bolker, & Walker, 2015). This approach was used to analyze the nested, repeated measures observations ($N = 85,659$ over $N = 18$ subjects); by using a hierarchical mixed logistic regression, the relative weights of each subjects measures is determined by both the sample size in the group and the variation of measures within and between groups (Gelman & Hill, 2007). In this way, a subject who had 1 night of data could be evaluated on the same “scale” in the regression model as a subject with 5 nights of data. In sum, the hierarchical mixed logistic regression model is a compromise between two extremes of statistical analysis that would either ignore the variation between the subjects or overstate the variation between subjects (Gelman & Hill, 2007).

Model Selection

Model selection began by establishing a reference model with nighttime awakenings as the outcome, and sequentially entering each predictor variable (sound, light, and movement) and confounding variable (GCS, ISS, age, and race) into the generalized linear mixed effects model as fixed effects. Best model fit was based on the Bayesian Inference Criterion (BIC), with a lower BIC indicating a better model.

Model Interpretation and Accuracy Analyses

Using the best fitting model, a predicted probability of nighttime awakenings was calculated based on the coefficients of the fixed effects (predictor variables). Coefficients were then resampled with replacement to obtain a measure of accuracy (upper and lower confidence intervals and p -values). Resampling with replacement was then conducted on an “intervention” dataset. This process provided perspective on how the predicted probability of nighttime awakenings would fluctuate when ambient stimuli are decreased; measures of accuracy were also found on the intervention dataset.

Significance Levels

A confidence interval of 95% was used to assess the likelihood of coefficients from the hierarchical mixed logistic regression being different from zero. A 95% confidence interval was used because it is a common indicator of significance across many disciplines. A p -value of 0.05 or less was set to indicate statistical significance for correlation associations and model fit.

RESULTS

Participant Characteristics

Owing to one sensor file having the wrong time stamp and to another sensor file being incomplete, the data of only 18 subjects were used in the final analysis (N= 18). The mean age of

subjects was 65 years ($SD = 17.5$). The average GCS was 9.1 ($SD = 4.9$) (see Table 1 for detailed participant characteristics). A GCS of 9.1 indicates that, overall, the sample had severe TBI.

Ambient Stimuli Description

Considering all levels of ambient exposure, study participants were likely to be awake for 24% of the time (nearly 3 hours) during the time they were monitored between the hours of 2000 and 0800. Overall, the sample was exposed to low light levels. Sound, light, and movement were highest at 2000 hours: 56.30 dB(A), 21.18 (lux), and 0.48(p), respectively. Average sound levels were lowest at 0300 hours [$M = 50$ dB(A)]. Average light and movement levels were lowest at 0200 hours ($M = 2$ (lux) and $M = 0.17$ (p), respectively).

Model Fit

The best reference model included “subject” and “subject * night of stay” as the main random effects. The best model fit showed that sound, light, and movement *collectively* lower the BIC scores. Conversely, night of stay, GCS, and age worsened the model. Therefore, the model that included sound, light, and movement as fixed effect was used; this is the model that will be explained hereafter (see Table 2).

Accuracy Analyses

In Table 3, model output shows that each stimulus made a statistically significant contribution to nighttime awakenings (all p -values < 0.001). To assign accuracy to these estimates, coefficients of each stimulus were randomly sampled with replacement and showed that light was not a statistically significant contributor to nighttime awakenings (CI, -0.001 to 0.000) as indicated by the p -value of the resampled data (p -value = 0.17). Descriptive results of the ambient stimuli can also be found in Table 3.

Predicted Probabilities of Nighttime Awakenings

Using the mean values of the predictor variables (sound, light, and motion) the regression model shows that there is a 20% probability of a subject waking up during the night (see Table 4). Table 3 shows both the “Reference” predicted probability and the “Intervention” predicted probability.

With all other variables set at their sample averages, a decrease in movement to “0” (indicating no movement in the subject’s room) decreases the probability of awakenings from 20% to about 15%; this is a change of about 5 percentage points, and is statistically significant (CI, 0.3–0.6). When sound levels were decreased by 5 dB(A) (MacLeod, Dunn, Busch-Vishniac, West, & Reedy, 2007) and with all other variables set at their sample averages, probability of awakenings decreased from 20% to 17.6%; this is a change of about 2 percentage points and is also statistically significant (CI, 0.1–0.3). Light exposure resulted in a slight decrease in probability of awakenings, but as with the actual estimates of sample coefficients, this contribution was not statistically significant.

DISCUSSION

Our data support the argument that nocturnal noise and human movement in the rooms of subjects with moderate and severe TBI *negatively* affect sleep by increasing the probability of nighttime awakenings. Because the movement component of the sensor was positioned in such a way that would not include patient movement (see Figure 1) and because the movement sensor could only detect human activity owing to PIR, we posit that the nocturnal activity in the room is likely coming from a hospital staff person. Also, given the hospital’s policy regarding visiting hours from friends and family member, it is unlikely that movement, during nighttime hours, in such close proximity to the patient can be attributed to a family member. Our main finding is consistent with the work of Thomas et al. (2012), which cites staff interruptions as a

main contributor to sleep quality. Of the three ambient stimuli evaluated in this study, movement appeared to have the greatest impact on the probability of nighttime awakenings. Sound also had an impact on the probability of nighttime awakenings, but to a lesser extent. Nevertheless, this finding is consistent with studies showing the relationship between sleep disturbance and sudden changes in sound pressure levels (Park et al., 2014; Stansfeld & Matheson, 2003).

Surprisingly, our research data did not support the claim that light has an impact on a patient's probability of awakening, a finding that contrasts with the literature (Giménez et al., 2017; Gooley et al., 2011). It could be the case that light levels in the current study were only evaluated during the nighttime period while other studies assessed light levels on a 24-hour basis, perhaps in effort to capture the data that aligned with the human beings 25 hour circadian rhythm. Because we were aware that patients on this unit did not stay for long amounts of time (Williams & Thompson, 2017, *in press*) the focus was not on circadian rhythm alignment. Moreover, our method of capture (actigraphy) could not fully speak to circadian rhythm alignment without extensive, co-signor analyses. The fact that our data did not support the claim that each additional day on the hospital unit subsequently decreases the patients' susceptibility to nighttime awakenings was also surprising; the rationale behind this hypothesis is that the patient becomes normalized to the pattern of ambient stimuli exposure in the hospital. Though surprising, our finding is consistent with similar studies that examine sleep and environmental exposure in hospitalized patients with cancer (Linder & Christian, 2011); in fact, in our study, night of stay was shown to be a poor predictor of nighttime awakenings.

Results of related studies that have explored sleep behavior show the utility of actigraphy in this population (Chiu, et al., 2013; Duclos et al., 2014); results from those studies

also show evidence of sleep pathology in this population. For example, they report poor sleep efficiency, hypersomnia, and poor rest/activity consolidation (Chiu et al., 2013; Duclos et al., 2014; Wiseman-Hakes et al., 2016).

Movement and Human Activity in Hospitalized Patients

Movement was the predictor variable with the largest effect size. Movement also made the most profound change in the predictive probability of nighttime awakenings by decreasing it from 20% to 15%. For this current study, movement was a proxy for human intervention or patient care by hospital staff.

That fact that movement was the most reliable predictor and that it was likely carried out by hospital staff in the current study is consistent with other studies where human intervention by hospital staff was reported as being disruptive (Gabor et al., 2003; Pellicane, 2014; Yoder et al., 2013). This disruption is not exclusive to the night shift: bedside nurses deliver about 200 minutes of direct patient care in a 10-hour shift (Hendrich, Chow, Skierczynski, & Lu, 2008). Furthermore, that most of the vital sign checks occurred among a less-acute patient sample in a study by Yoder et al. (2013) may perhaps suggest the futility of nighttime patient care disruptions. Another study showed that 7–8 patient care activities occurred per hour among hospitalized ICU patients; these activities were responsible for about 7.1% of total arousals and awakenings (Gabor et al., 2003).

The highest level of movement occurred near the start of the 12-hour night shift (2000 hours) and we hypothesize that this is likely due to the shift change. Elevated noise, light, and patient care activity have also been noted at the start of the nursing shift by Linder & Christian (2011) and Uğraş et al. (2015). Conversely, the lowest levels of movement in the current study occurred at 0300 hours, which suggests that no or minimal patient care activity is occurring.

Uğras et al.(2015) support this concept of a “lull” time of the night, in that no patient care took place during this hour of the night in their study.

Noise and Nighttime Awakenings

To maintain sleep quality in general, nightly noise levels should not exceed 42 dB(A) (WHO, 2009). However, the average sample estimate of sound pressure level in the current study was well beyond that threshold. Our analysis also showed a statistically significant relationship between nighttime awakenings (sleep parameter) and sound pressure levels. Our results are consistent with literature that shows sound as a significant contributor to nighttime awakenings (Buxton et al., 2012) and demonstrates that noise has high and low fluctuations over the course of the night (Linder & Christian, 2011, 2012).

In contrast, the results are mildly inconclusive with regard to noise and other external factors serving as salient contributors to sleep disturbance among hospitalized patients (Alway, Halm, Shilhanek, & St Pierre, 2013). In several studies, results of objective stimulus exposure and sleep did not always support subjective assessments of sleep being poor due to noxious exposure to stimuli (Gathecha et al., 2016; Thomas et al., 2012). For instance, while hospitalized patients reported noise as a main contributor to their poor sleep on a subjective instrument, a significant relationship was not found between the actigraphy and sound pressure level assessments that were collected during the same study period (Thomas et al., 2012).

Noise may have likely had a lesser impact on sleep quality than movement because the current study used average background noise recordings, as opposed to an assessment that evaluated peaks of noise levels. Results from other studies that evaluated noise suggest that the latter method does a better job at capturing exposure variability (Neitzel, Stover, & Seixas, 2011). The former method was chosen in the current study to provide a baseline profile of the

sound pressure levels common to the unit studied. In fact, none of the variables in the current study evaluated peaks. All of the variables in the study examined the baseline levels of sound, light, and movement during the nighttime hours. This was an important component of the research because different units within a hospital have different patterns of sound pressure level exposure (Kracht, Busch-Vishniac, & West, 2007; Orellana, Busch-Vishniac, & West, 2007). Furthermore, the alarms that are often cited as primary sources of noise pollution in the hospital occur infrequently and are not particularly representative of frequency spectra of most hospital units (Busch-Vishniac, 2015; Busch-Vishniac et al., 2005).

Light Exposure: Not Significant

It was surprising that light was not a significant contributor to nighttime awakenings: we expected that the presence of artificial light would alter rest/activity cycles. Results from light interventions by Gooley et al. (2011) suggest that light should have had an effect on sleep and its related processes, even when lux levels were low (3 lux to 199 lux). The average sample estimate of lux in the current study was 9. Perhaps evaluating the relationship between light exposure and sleep in hospitalized patients requires data from both daytime and nighttime periods (Bernhofer, Higgins, Daly, Burant, & Hornick, 2014). It is also possible that nighttime awakenings were not the best sleep parameter to use to assess this association. In the study by Giménez et al. (2017), sleep onset latency was found to have a stronger association with light than nighttime awakening; however, this may not be feasible in subjects like those described in the current study because one cannot reliably assess when a hospitalized patient awakes in the morning or when they go to sleep at night.

Night of Stay

Our evidence did not support the hypothesis that the night of stay would be important in predicting the number of nighttime awakenings per patient. This was surprising, because we anticipated the patient would become desensitized to the care environment or that less intervention would be required as the patient condition improved. We speculated that variations in sleep behavior would occur over the course of hospitalization based on Keenan and Joseph's (2010) work, which suggests a difference in care delivery flow when the patient with TBI steps down from the ICU to an intermediate care unit. However, other studies assessing sleep and ambient stimuli found that there was a night of stay effect (Gathecha et al., 2016; Giménez et al., 2017). One explanation for the current finding could be that patients in the current study had a shorter length of stay than those in prior studies, as well as varying levels of medical acuity.

Limitations

The most notable limitation is the inability to explicitly attribute “movement” solely to a hospital staff member entering or exiting the room. The analysis did not account for patients housed in semi-private rooms with a roommate. The assumption is that the motion sensor will not be triggered by patients based on sensor positioning (see Figure 1), but because not directly observed, we cannot state this with complete assurance. A further limitation is that this study was conducted at a single institution and is therefore not generalizable. However, the within-person focus of this analysis may mitigate the extent of this limitation. Due to the novelty of this research area, these findings are not likely transferrable to other hospitalized patient populations; however, it can be a starting point for future investigations.

Strengths and Methodological Considerations

The multi-level logistic model was used to address the nested, repeated observations (scheme: “observations within subjects within nights”; Gelman & Hill, 2007). This analysis assigned equitable weighting for each subject’s observations. Resampling techniques proved to be an integral component of this study’s analysis because they helped to establish measures of accuracy that the multilevel model regression model could not inherently produce.

Furthermore, a conservative model was fit such that predictor variables (sound, light, and movement) were entered as fixed effects and subjects and subject-night interactions were the random effects. This varying-intercept model is parsimonious and aligns with the aims of this study. The outcome variable—nighttime awakenings—was chosen because it was thought to correspond well with patterns of exposure to ambient stimuli and their possible impact.

The quality of the data (quantity and granularity of the actigraphy and sensor) seems sufficient in its ability to reliably address specific questions related to the study’s variables. The Actiwatch and multisensor both seem to demonstrate face validity and construct validity, especially the sensor, which was designed for this study. Moreover, the ambient stimuli outlined in this current study have been variables of interest in other studies aimed at objectively monitoring the environment of hospitalized patients (Buxton et al., 2012; Desjardins, Cardinal, Belzile, & McCusker, 2008; Giménez et al., 2017). Nevertheless, this was not an observational study that utilized participant-observer methods to uncover the source of sound, light, and movement. Not having observational data limits the extent of the conclusions for the purpose of developing a nursing intervention.

CONCLUSIONS

Movement—as with care provision or other human intervention—and sound are the most important contributors to sleep disturbance among hospitalized intermediate care patients

with moderate and severe TBI. Surprisingly, light exposure did not make a significant contribution to sleep disturbance in this sample. Implementation of longitudinal sensors that characterize the patient's exposure to the ambient stimuli can also be important; moreover, the method to capture ambient stimuli in the current study was novel and innovative. The information gleaned from this type of technology can serve as the basis for patient and unit-specific policy investigations into workflow patterns/human interventions (Kartakis, Sakkalis, Tourlakis, Zacharioudakis, & Stephanidis, 2012). But as a consideration, the study cannot inform interventions outright because it did not utilize observational methods.

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Tables

Table. 4.1 *Demographic Characteristics of Intermediate-care Patients with TBI on Neuroscience Unit (n=18)*

Measure	<u>n</u>	<u>%</u>
Male	14	77
White	17	94
Marital status		
<i>Single</i>	5	27
<i>Married</i>	5	27
<i>Widow/Widower</i>	3	16
<i>Cohabiting</i>	3	16
<i>Divorced</i>	2	11
Had health insurance	16	88
	<i>M</i>	<i>SD</i>
Average nightly length of stay on unit	3.3	1.6
Glasgow Coma Scale Score (GCS)	9.1	4.8
Patient Age	65.3	17.4

Note. The GCS used for this study was obtained from initial note in the emergency department.

Table 4.2. Sequential Entry of Model Selection and corresponding Bayesian Inference Criterion (BIC) value

Model	BIC
Base model: (1 Subject/Night)	82 682
Base model + Sound	80 079
Base model + Light	82 080
Base model + Movement	77 069
Base model + Sound + Movement	76 614
Base model + Sound + Light	79 910
Base model + Movement + Light	76 968
Base model + Sound + Light + Movement	76 578
Base model + Sound + Light + Movement + Age	76 589
Base model + Sound + Light + Movement + GCS	76 586

Table 4.3. Multi-level Model Output with Resampled Coefficients & their Confidence Intervals

Fixed Effects		<i>B</i>			<i>M</i>	<i>Range</i>
(Intercept)	-3.4				0.24	0 - 1
Nighttime Awakenings (p)						
Stimulus		<i>Model</i>	<i>Resampled</i>	<i>Resampled</i>	<i>M</i>	<i>Range</i>
		<i>p-value</i>	<i>p-value</i>	<i>CI (95%)</i>		
Sound (dB(A))	0.031	$p < 0.001$	$p = 0.005$	(0.15 -- 0.45)	52	41 - 128
Light (lumens)	0.002	$p < 0.001$	$p = 0.17$	(-0.001 – 0.001)	9	0 - 330
Movement (p)	1.22	$p < 0.001$	$p = 0.005$	(0.93 -- 0.150)	0.28	0 - 1

Note. Model coefficients were standardized to assist with convergence in [R]Studio.

Table 4.4. Predicted Probabilities of Nighttime Awakenings

<i>Reference</i>				
Sound (dB(A))	Light(Lux)	Motion (p)	<i>Pr</i>	
52	9	0.28	0.201	
<i>Intervention</i>				
Sound (dB(A))	Light(Lux)	Motion (p)	<i>Pr</i> (Δ from reference)	CI (2.5% - 97.5%)
47	9	0.28	0.176 (Δ 0.024)	(0.1 – 0.3)
52	2	0.28	0.198 (Δ 0.002)	(-0.001 - 0.0001)
52	9	0	0.151 (Δ 0.049)	(0.3 – 0.6)

Figures

Figure 4.1. Location of multisensor in a subjects' room indicated by an "X" (multisensor not shown here)



CHAPTER 5: CONCLUSION

This research helps to further understanding about the sleep of patients with moderate and severe traumatic brain injury (TBI) during their hospitalization in an intermediate care setting. Sleep was defined according to parameters of nurse-reported sleep quality (chapter 2), wake bouts, total wake time, and sleep efficiency (chapter 3), and percent of nighttime awakenings (chapter 4). Though characterized in different ways in each chapter, capturing the frequency and influence of nighttime awakenings in this target population was the focus of this entire dissertation.

In chapter 1, I articulated the public health concerns relating to the need to focus on patients hospitalized in intermediate care units with moderate and severe TBI. I also conveyed factors of nighttime awakenings with intrinsic and extrinsic origins which compromise the quality of sleep in this patient population. Extrinsic factors included aspects of the hospital milieu like exposure to ambient sound, light, and movement by others. Before we could explore the influence of ambient stimuli (sound, light, and movement by others) on the patient's sleep, it was important to better understand the frequency of their care during the nighttime hours their hospital stay. This was accomplished by the retrospective chart review of Chapter 2.

In chapter 2, I examined how nurse-reported sleep quality (per the nurses' note) was associated with night time care activities. The premise here was that nighttime care activities, though important, still had the potential to disrupt the patient from their nighttime sleep. Though it there was a weak association between nighttime care activities and sleep quality, the evidence suggested that further exploration maybe necessary; especially consideration that fact that nearly 6 nighttime awakenings occurred (on average) during the nighttime hours of subjects in the sample and that nearly all the sample "slept well" for less than half the nights of the 7 day data

extraction period. Therefore, evaluating sleep with a more objective method was the priority in chapter 3 where nighttime awakenings were elucidated with the number of wake bouts, the total time a patient spent awake (in minutes) and the patient's sleep efficiency. Unlike chapter 1, the sleep quality data came from wrist actigraphy and not from the nurse's note. Finally in chapter 4, attempting to capture the ambient stimuli that influenced the probability of nighttime awakening helped to paint a clearer picture of what the patient's perceived sleep environment might be like.

The novel aspect of this dissertation was the pragmatic data collection of sound, light and motion stimuli in a single device. That fact that I could install the multi-sensor in the patient's room and let it run by itself was important because its presence was not a hindrance to patient-care. Also, the fact that the data was locally collected and did not require Wi-Fi access prevented the need to establish safeguards against the patients' health information being compromised. Additionally, the methodological bonus of the multi-sensor is that it collected all of these stimuli on a single device which omitted the need to match time stamps of several devices. Despite the fact this dissertation did not utilize participant-observation methods, using the multi-sensor was a way to collect objective environmental data about a phase of hospitalization that is understudied for this target population. If nothing else, the evidence in my dissertation serves as a basis for further exploration.

With this dissertation, we are able to at least say that there is a specific pattern of exposure in sound, light, and motion those patients in this phase of hospitalization experience (Kartakis et al., 2012). Though Gooley et al. (2011), Buxton et al (2012), and Giménez et al., (2017) have each explored one or two of these stimuli, none of the studies have explored all three. Also, these studies have not focused on the intermediate care phase of hospitalization.

Moreover, while Chiu et.al (2013) and Duclos et al., (2014) have explored sleep in this patient population, there was no incorporation of ambient stimuli exposure.

There were two main contradictory findings. The first was that light was not a reliable predictor of nighttime awakenings despite similar studies that explored the influence of light on sleep in human beings; these studies explored sleep in hospital and sleep laboratory settings (see Chapter 4) (Gathecha et al., 2016; Giménez et al., 2017; Gooley et al., 2011). The second contradiction was that functional outcome could not be predicted by poor sleep (see Chapter 3). There was no association between any of the injury variables and sleep parameters except for wake bouts and the Rancho Los Amigo (RLA) cognitive functioning scale. Studies by Sullivan et al. (2016) and Sandhaug et al. (2010) suggest that functional outcome is an important factor in the sleep of patients following a TBI.

The contradictory result may be due to lack of variability in the samples measures (FIM and sleep parameters); it may also be due to the small sample size (N= 17). Perhaps in the future, I would consider using other measures that capture disability because a study were a modified Rankin Score was used to assess disability in patient with moderate and severe TBI was able to show that consolidated sleep *could* improve functional outcome in a patient with moderate and severe TBI (Sandsmark et al., 2016). It should be noted, however, that Sandsmark et al. (2016) utilized a more rigorous method of objective sleep assessment—continuous electroencephalogram. In the same vein, I would also consider evaluating the full 24 hour period of rest/activity patterns using a more rigorous, yet more costly, method like polysomnography as did Wiseman-Hakes et al. (2016) in their study of ICU-bound patients with moderate and severe TBI. The evidence for exploring the sleep disturbance, functional outcome relationship in the intermediate care phase of patients with moderate and severe TBI has been demonstrated in Chiu

et al. (2014); in that study they found that patients with TBI in an intermediate care setting showed stronger associations between their sleep parameters and cognitive outcomes (Chiu et al., 2014). Furthermore, Nelson et al. (2015) showed that the nursing workload on the neuroscience specialty intermediate care unit is unique enough from other intermediate care floors and from the neuro ICU to warrant its own evidence. Finally, I did not consider the anatomical location of injury. This is important for future studies as injuries in different parts of the neuroanatomy can affect the networks responsible for sleep regulation.

The evidence in chapters 2, 3, and 4, show that patients with moderate and severe TBI receiving care in an intermediate hospital care setting have nighttime experiences that is worth further investigation and intervention. Perhaps disturbed sleep could be an indication of a poorer therapeutic environment and altering the patient's room environment may be beneficial to the patient's recovery. Altering the room environment can subsequently decrease likelihood of nighttime disturbances. However, this is just the tip of the iceberg and studies utilizing participant-observer methods (for chapter 2 and chapter 4) and polysomnography (for chapter 3) are important to continue to develop the program of research in this target population next steps.

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Appendix (contains [R] code for chapter 3 and chapter 4)**Chapter 3 Code**

```

rm(list=ls())
getwd()
setwd("C:/Users/etw89/Documents/Analysis")

SleepOnly <- read.csv(file = "SleepOnlyDataMinusOneFiveandThirteen.csv",
header = TRUE)
library("psych")
library("dplyr")
library("ggplot2")
library("Hmisc")
library("lubridate")
library("lme4")
#####

SleepOnly <- SleepOnly[c("ID", "RLA", "FIM", "Gender", "AGE", "GCS", "ISS",
"Start.Time", "End.Time", "Start.Date", "Start.Day", "End.Date",
"End.Day",
"X.Wake.Bouts", "Efficiency...", "Wake.Time.minutes.",
"Interval.", "Interval.Type")]

SleepOnly$Start.Date <- as.POSIXct(SleepOnly$Start.Date, format = "%m/%d/%Y")
SleepOnly$End.Date <- as.POSIXct(SleepOnly$End.Date, format = "%m/%d/%Y")

SleepOnly$Start.Time <- as.POSIXct(SleepOnly$Start.Time, format = "%H:%M:%S")
SleepOnly$End.Time <- as.POSIXct(SleepOnly$End.Time, format = "%H:%M:%S")

names(SleepOnly)[14] <- "WB"
names(SleepOnly)[15] <- "SleepEff"
names(SleepOnly)[16] <- "TWT"
names(SleepOnly)[17] <- "Night"

###
psych::describe(SleepOnly[c("Night", "WB", "SleepEff",
" TWT", "AGE", "GCS", "RLA",
" ISS", "Gender", "FIM")])

###
df3 <- as.data.frame(SleepOnly[c("Night", "WB", "SleepEff",
" TWT", "AGE", "GCS", "RLA",
" ISS", "Gender")])

print(corr.test(df3, method = "pearson"), short = FALSE)

```

```

####
correlations <- rcorr(as.matrix(df3), type = "pearson")

correlations

###

WBmlm <- lmer(WB ~ AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(WBmlm)
summary(WBmlm)

WBgcs <- lmer(WB ~ GCS + AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(WBgcs)
summary(WBgcs)

WBiss <- lmer(WB ~ ISS + AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(WBiss)
summary(WBiss)

WBrLA <- lmer(WB ~ RLA + AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(WBrLA)
summary(WBrLA)

anova(WBmlm, WBgcs)
anova(WBmlm, WBiss)
anova(WBmlm, WBrLA)

###
SleepEffMlm<- lmer(SleepEff ~ AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(SleepEffMlm)

SleepEffGCS<- lmer(SleepEff ~ GCS + AGE + (1|ID), REML = FALSE, data =
SleepOnly)
BIC(SleepEffGCS)
summary(SleepEffGCS)

SleepEffGender <- lmer(SleepEff ~ Gender + AGE + (1|ID), REML = FALSE, data
= SleepOnly)
BIC(SleepEffGender)

SleepEffRla <- lmer(SleepEff ~ RLA + AGE + (1|ID), REML = FALSE, data =
SleepOnly)
BIC(SleepEffRla)

```

```

SleepEffiss <- lmer(SleepEff ~ ISS + AGE + (1|ID), REML = FALSE, data =
SleepOnly)
BIC(SleepEffiss)

anova(SleepEffMlm, SleepEffGCS)
anova(SleepEffMlm, SleepEffGender)
anova(SleepEffMlm, SleepEffRla)
anova(SleepEffMlm, SleepEffiss)

###
TWTmlm <- lmer(TWT ~ AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(TWTmlm)
summary(TWTmlm)

TWTGcs <- lmer(TWT ~ GCS + AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(TWTGcs)
summary(TWTGcs)

TWTiss <- lmer(TWT ~ ISS + AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(TWTiss)
summary(TWTiss)

TWTrLA <- lmer(TWT ~ RLA + AGE + (1|ID), REML = FALSE, data = SleepOnly)
BIC(TWTrLA)

anova(TWTmlm, TWTGcs)
anova(TWTmlm, TWTiss)
anova(TWTmlm, TWTrLA)

###
#Aggregating data to run FIM

#Aggregating sleep parameters by mean
SleepOnlyAggyMeans <- SleepOnly %>% group_by(ID)%>% summarise(FIM =
mean(FIM), Age = max(AGE), Sex = max(Gender), TWT = round(mean(TWT)),
SleepEff = round(mean(SleepEff)), WB = round(mean(WB)), RLA = mean(RLA), GCS
= mean(GCS), ISS = mean(ISS), Night = max(Night))

#Aggregating sleep parameters by median
SleepOnlyAggyMedian <- SleepOnly %>% group_by(ID)%>% summarise(FIM =
mean(FIM), Age = max(AGE), Sex = max(Gender), TWT = round(median(TWT)),
SleepEff = round(median(SleepEff)), WB = round(median(WB)), RLA = mean(RLA),
GCS = mean(GCS), ISS = mean(ISS), Night = max(Night))

#Correlation ##Aggy Means
psych::describe(SleepOnlyAggyMeans[c("Night", "WB", "SleepEff",
"TWT", "FIM", "Age", "Sex")])

###
dfAggyMeans <- as.data.frame(SleepOnlyAggyMeans[c("Night", "WB", "SleepEff",

```

```

      "TWT", "FIM", "Age", "Sex"]])

print(corr.test(dfAggyMeans, method = "pearson"), short = FALSE)

####
AggyMeansCorrelations <- rcorr(as.matrix(dfAggyMeans), type = "pearson")

AggyMeansCorrelations

#Correlation ##Aggy Median
psych::describe(SleepOnlyAggyMedian[c("Night", "WB", "SleepEff",
                                       "TWT", "FIM", "Age", "Sex")])

###
dfAggyMedian <- as.data.frame(SleepOnlyAggyMedian[c("Night", "WB",
                                                    "SleepEff",
                                                    "TWT", "FIM", "Age", "Sex")])

print(corr.test(dfAggyMedian, method = "pearson"), short = FALSE)

####
AggyMediansCorrelations <- rcorr(as.matrix(dfAggyMedian), type = "pearson")

AggyMediansCorrelations

#OLS functions
#Variable Name <- lm(Outcome Variable ~ Predictor Variable, data = Dataframe)

##AggyMeans
AggyMeans_FIMwakeBouts <- lm(FIM ~ WB + Age, data = SleepOnlyAggyMeans)
summary(AggyMeans_FIMwakeBouts)

AggyMeans_FIMtotalWakeTime <- lm(FIM ~ TWT + Age, data = SleepOnlyAggyMeans)
summary(AggyMeans_FIMtotalWakeTime)

AggyMeans_FIMsleepEff <- lm(FIM ~ SleepEff + Age, data = SleepOnlyAggyMeans)
summary(AggyMeans_FIMsleepEff)

##AggyMedians
AggyMedians_FIMwakeBouts <- lm(FIM ~ WB + Age, data = SleepOnlyAggyMedian)
summary(AggyMedians_FIMwakeBouts)

AggyMedians_FIMtotalWakeTime <- lm(FIM ~ TWT + Age, data =
SleepOnlyAggyMedian)
summary(AggyMedians_FIMtotalWakeTime)

AggyMedians_FIMsleepEff <- lm(FIM ~ SleepEff + Age, data =
SleepOnlyAggyMedian)
summary(AggyMedians_FIMsleepEff)

```

```

#Night 1 analysis Only; AggyNightOne

SleepOnlyAggyNightOne <- SleepOnly %>% group_by(ID)%>% filter(Night ==
min(Night))%>% summarise(FIM = mean(FIM), Age = max(AGE), Sex = max(Gender),
TWT = max(TWT), SleepEff = max(SleepEff), WB = max(WB))

psych::describe(SleepOnlyAggyNightOne[c("WB", "SleepEff",
                                         "TWT", "FIM", "Age", "Sex")])

###
dfAggyNightOne <- as.data.frame(SleepOnlyAggyNightOne[c("WB", "SleepEff",
                                                         "TWT", "FIM", "Age",
                                                         "Sex")])

print(corr.test(dfAggyNightOne, method = "pearson"), short = FALSE)

####
AggyNightOneCorrelations <- rcorr(as.matrix(dfAggyNightOne), type =
"pearson")

AggyNightOneCorrelations

#OLS functions
#Variable Name <- lm(Outcome Variable ~ Predictor Variable, data = Dataframe)

AggyNightOne_FIMwakeBouts <- lm(FIM ~ WB + Age, data = SleepOnlyAggyNightOne)
summary(AggyNightOne_FIMwakeBouts)

AggyNightOne_FIMtotalWakeTime <- lm(FIM ~ TWT + Age, data =
SleepOnlyAggyNightOne)
summary(AggyNightOne_FIMtotalWakeTime)

AggyNightOne_FIMsleepEff <- lm(FIM ~ SleepEff + Age, data =
SleepOnlyAggyNightOne)
summary(AggyNightOne_FIMsleepEff)

#WB and FIM Night one graphs
MA <- ggplot(SleepOnlyAggyNightOne, aes(x= WB, y= FIM))
MA <- MA + geom_point(shape=10, size=5) + xlab("Wake Bouts (#)") +
ylab("FIM") + geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM
and Wake Bouts(#) Night 1")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
                 axis.text=element_text(size=20, color="black"))
MA + mytheme
MA <- MA + mytheme

```

```

AAA <- ggplot(SleepOnlyAggyNightOne, aes(x= TWT, y= FIM))
AAA<- AAA + geom_point(shape=10, size=5) + xlab("Total Wake Time") +
ylab("FIM") + geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM
and Total Wake Time Night 1")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
axis.text=element_text(size=20, color="black"))
AAA + mytheme
AAA <- AAA + mytheme

BBB <- ggplot(SleepOnlyAggyNightOne, aes(x= SleepEff, y= FIM))
BBB <- BBB + geom_point(shape=10, size=5) + xlab("Sleep Eff.") + ylab("FIM")
+ geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM and Sleep
Eff., Night 1")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
axis.text=element_text(size=20, color="black"))
BBB+ mytheme
BBB <- BBB + mytheme

#WB and FIM Aggregated Mean graphs
ZZZ <- ggplot(SleepOnlyAggyMeans, aes(x= WB, y= FIM))
ZZZ <- ZZZ + geom_point(shape=10, size=5) + xlab("Wake Bouts (#)") +
ylab("FIM") + geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM
and Wake Bouts(#) Aggregated Mean")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
axis.text=element_text(size=20, color="black"))
ZZZ + mytheme
ZZZ <- ZZZ+ mytheme

YYY <- ggplot(SleepOnlyAggyMeans, aes(x= TWT, y= FIM))
YYY <- YYY + geom_point(shape=10, size=5) + xlab("Total Wake Time") +
ylab("FIM") + geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM
and Total Wake Time Aggregated Mean")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
axis.text=element_text(size=20, color="black"))
YYY + mytheme
YYY<- YYY + mytheme

XXX <- ggplot(SleepOnlyAggyMeans, aes(x= SleepEff, y= FIM))
XXX <- XXX + geom_point(shape=10, size=5) + xlab("Sleep Eff.") + ylab("FIM")
+ geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM and Sleep
Eff., Aggregated Mean")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
axis.text=element_text(size=20, color="black"))
XXX + mytheme

```

```

XXX <- XXX + mytheme

#Median
RRR <- ggplot(SleepOnlyAggyMedian, aes(x= WB, y= FIM))
RRR <- RRR + geom_point(shape=10, size=5) + xlab("Wake Bouts (#)") +
ylab("FIM") + geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM
and Wake Bouts(#), Aggregated Median")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
                axis.text=element_text(size=20, color="black"))
RRR + mytheme
RRR <- RRR + mytheme

SSS <- ggplot(SleepOnlyAggyMedian, aes(x= TWT, y= FIM))
SSS <- SSS + geom_point(shape=10, size=5) + xlab("Total Wake Time") +
ylab("FIM") + geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM
and Total Wake Time, Aggregated Median")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
                axis.text=element_text(size=20, color="black"))
SSS + mytheme
SSS <- SSS + mytheme

TTT <- ggplot(SleepOnlyAggyMedian, aes(x= SleepEff, y= FIM))
TTT <- TTT + geom_point(shape=10, size=5) + xlab("Sleep Eff.") + ylab("FIM")
+ geom_smooth(method=lm, se=TRUE, color="blue") + ggtitle("FIM and Sleep
Eff., Aggregated Median")
mytheme <- theme(axis.title=element_text(size=20),
title=element_text(size=20),
                axis.text=element_text(size=20, color="black"))
TTT + mytheme
TTT <- TTT + mytheme

```


Chapter 4 Code

Base Functions for Transforming Data

```
#make a function to delete all "NaN" in the dataframe of actigraphy

any.nan <- function(newrow){
  before.nan <- is.na(as.matrix(newrow))
  after.nan <- any(before.nan)
  return(after.nan)
}

#make a function to preprocess actigraphy data: remove NaN, rename columns,
#change time variable from factor to POSIXct
preprocess.nan12to24HRS <- function(filename, skip.1){
  unprocess.data <- read.csv(filename, skip = skip.1)
  unprocess.data <- unprocess.data[, 1:13]
  na.indica <- apply(unprocess.data,1,any.nan)
  process.data <- unprocess.data[na.indica == 0, ]
  colnames(process.data) <- c("Line", "Day", "Date", "Time", "Offwrist",
                             "Activity","Marker",
"whiteLight","redLight","greenLight",
                             "blueLight", "SleepWake", "IntervalStatus")
  process.data$datetime <-as.POSIXct(paste(process.data$Date,process.data$Time),
format = "%m/%e/%YI:%M:%S %p")
  return(process.data)
}

#making a function that works for the actigraphy data that is already on a 24
hr scale
preprocess.nan24to24HRS <- function(filename, skip.1){
  unprocess.data <- read.csv(filename, skip = skip.1)
  unprocess.data <- unprocess.data[, 1:13]
  na.indica <- apply(unprocess.data,1,any.nan)
  process.data <- unprocess.data[na.indica == 0, ]
  colnames(process.data) <- c("Line", "Day", "Date", "Time", "Offwrist",
                             "Activity","Marker",
"whiteLight","redLight","greenLight",
                             "blueLight", "SleepWake", "IntervalStatus")
  process.data$datetime <-as.POSIXct(paste(process.data$Date,process.data$Time),
format = "%m/%e/%Y%H:%M:%S")
  return(process.data)
}

#make a function to preprocess protoport data: read in file, provider header,
set to 24 HRS time, re-code NA's in LUX to "0", remove duplicates
preprocess.sensor <- function(filename){
  unprocess.sensor <- read.csv(filename, header = FALSE)
  colnames(unprocess.sensor)<- c("datetime", "LUX", "MOVE", "SOUND")
  unprocess.sensor$datetime <- as.POSIXct(unprocess.sensor$datetime, format =
"%m/%e/%Y %H:%M:%S" )
}
```

```

    unprocess.sensor$LUX[(is.na(unprocess.sensor$LUX))] <- 0
    pross.sensor <- subset(unprocess.sensor,
!duplicated(unprocess.sensor$datetime))
    return(pross.sensor)
}

#aggregating protoport data to 30 sec intervals

#agg.time <- function(sensor.agg){
#pre.agg <- cut(sensor.agg$datetime, breaks = "30 sec")
#post.agg.sensor <- aggregate(x= sensor.agg, by= list(pre.agg), FUN = mean)
#return(post.agg.sensor[, -1])
#}

#deluxe
agg.time.deluxe <- function(sensor.data, acti.data){
  ## make min and max the same!

  bins <- cut(c(sensor.data$datetime, acti.data$datetime), breaks = "30 sec")
  bins.sensor <- bins[1:nrow(sensor.data)]
  bins.acti <- bins[(nrow(sensor.data) + 1):length(bins)]

  sensor.agg <- aggregate(x = sensor.data, by = list(bins.sensor), FUN = max)
  colnames(sensor.agg)[1] <- "time.bin"
  acti.agg <- aggregate(x = acti.data, by = list(bins.acti), FUN =
function(x){x})
  #acti.agg <- aggregate(x = acti.data[,5:12], by = list(bins.acti), FUN =
mean)
  colnames(acti.agg)[1] <- "time.bin"

  full.data <- inner_join(sensor.agg, acti.agg, by = "time.bin")
  return(full.data)
}

FilterNightIndicies <- function(Full.Data){
  Full.Data$Night <- 0
  Full.Data$time2 <- ymd_hms(Full.Data$datetime.x)
  #Full.Data$time2 <- ymd_hms(Full.Data$datetime)
  Full.Data$New_time <- Full.Data$time2 + 4*60*60
  Full.Data$Night <- yday(Full.Data$New_time)
  Full.Data$Night <- Full.Data$Night - Full.Data$Night[1]
  nday <- max(Full.Data$Night)
  SUBSET <- NULL
  for ( i in 1:nday) {
    DAY <- Full.Data[Full.Data$Night==i, ]
    #make sure to use hours () function
    N1 <- DAY[hour(DAY$time2)>= 20,]
    N2 <- DAY[hour(DAY$time2)< 8, ]

    NN <- rbind(N1, N2)
    SUBSET <- rbind(SUBSET, NN)
  }
  return(SUBSET)
}

```

```

}

#Script to create aggregated dataframes from NON agg data;

rm(list=ls())
#load packages
library("dplyr")
library("lubridate")
library("lme4")
library("MASS")
library("arm")
library("Hmisc")
# read in non-aggregated data file
setwd("C:/Users/Ellita/Documents/Analysis")
NonAggData <- read.csv(file = "NonAggData.csv", header = TRUE)

#first create new col for new timestep as opposed to factor/char vector

NonAggData <- dplyr::select(NonAggData, -Scale.maxLUX, -Scale.maxMOVE, -
Scale.maxSOUND) %>%
  mutate(newtimestamp = mdy_hm(Time))

#create a col for hour
NonAggData$clockHour <- hour(NonAggData$newtimestamp)

#group by hour in the night

NightHourPeople <- group_by(NonAggData, ID, Night, clockHour) %>%
  summarise(sound = mean(maxSOUND), light = mean(maxLUX), motion =
mean(maxMOVE))

#group by hour
HourPeople <- group_by(NonAggData, ID, clockHour) %>%
  summarise(sound = mean(maxSOUND), light = mean(maxLUX), motion =
mean(maxMOVE))

#group by hour no ppl
HourNOTPeople <- group_by(NonAggData, clockHour) %>%
  summarise(sound = mean(maxSOUND), light = mean(maxLUX), motion =
mean(maxMOVE))

#Script to get confidence intervals and histograms of bootstrap, non-agg-data
rm(list = ls())
setwd("C:/Users/Ellita/Documents/Analysis")
getwd()

#script to make the TestBootOUTPUT.csv
##MUST SOURCE IN:

#source("Code/BootstrapFunctions.r")

```

```

##Must build dfSE which is where you put your intervention levels of ambient
stimuli

#a <- c(52, 9, 0.28)
#b <- c(47, 9, 0.28) # decrease by 5 db
#c <- c(52, 2, 0.28) # decrease to 2 lumens
#d <- c(52, 9, 0) # decrease from 28% movement to no movement
#
#magicSE <- rbind(a,b,c,d)
#dfSE <- as.data.frame(magicSE)
#colnames(dfSE) <- c("maxSOUND", "maxLUX", "maxMOVE")

#How to call these functions (in order of appearance in
"Code/BootstrapFunctions.r" R[Studio] file):

#1. AnalysisofNonAgg(NonAggdata, dfSE)

#2. Bootstrapline(NonAggdata)

#3. TestBootDist <- BootStrapDist(NonAggdata, 200, dfSE)

###Always run the next two lines TOGETHER!!!!
#set.seed(1) # tells [r] to set my randomness to start at one. This helps
with reproducibility.
#TestBootDist <- BootStrapDist(NonAggdata, 200, dfSE)
#write.csv(TestBootDist, "TestBootOUTPUT.csv")

#Now, you can analyze....
TestBootDistIntro <- read.csv("TestBootOUTPUT.csv", header = TRUE)

TestBootDist <- TestBootDistIntro[ , -c(1)]

colnames(TestBootDist)<- c("Sound", "Light", "Motion")

hist(TestBootDist[, 1])
quantile(TestBootDist[, 1], c(0.025, 0.975))

hist(TestBootDist[, 2])
quantile(TestBootDist[, 2], c(0.025, 0.975))

hist(TestBootDist[, 3])
quantile(TestBootDist[, 3], c(0.025, 0.975))

rm(list = ls())
library(dplyr)
library(lubridate)
library(lme4)
library(MASS)
library(mlmRev)
library(arm)

```

```

setwd("C:/Users/Ellita/Documents/Analysis")

source("Code/Functions.r") #preprocess

acti_filenames <- c("Data/001.csv", "Data/002.csv", "Data/003.csv",
                  "Data/004.csv", "Data/005.csv", "Data/006.csv",
                  "Data/007.csv", "Data/008.csv", "Data/009.csv",
                  "Data/010.csv", "Data/011.csv", "Data/013.csv",
                  "Data/014.csv", "Data/015.csv", "Data/016.csv",
                  "Data/018.csv", "Data/019.csv", "Data/020.csv")

sensor_filenames <- c("Data/GN001.TXT", "Data/GN002.TXT", "Data/GN003.TXT",
                    "Data/GN004.TXT", "Data/GN005.TXT", "Data/GN006.TXT",
                    "Data/GN007.TXT", "Data/GN008.TXT", "Data/GN009.TXT",
                    "Data/GN010.TXT", "Data/GN011.TXT", "Data/GN013.TXT",
                    "Data/GN014.TXT", "Data/GN015.TXT", "Data/GN016.TXT",
                    "Data/GN018.TXT", "Data/GN019.TXT", "Data/GN020.TXT")

skippy_vector <- c(146,134,148,
                  148,133,138,
                  150,150,155,
                  144,136,146,
                  153,158,150,
                  148,146,138)

Tweleve.or.24HRS <- c(12,12,12,
                    12,12,12,
                    12,12,12,
                    12,12,24,
                    24,24,24,
                    24,24,24)

patient.id <- c(001,002,003,
               004,005,006,
               007,008,009,
               010,011,013,
               014,015,016,
               018,019,020)

CompleteData <- NULL

#Forloop to bind all patient
for(pt.id in 1:18){
  if(Tweleve.or.24HRS[pt.id]==12) {
    acti<- prepross.nan12to24HRS(acti_filenames[pt.id],
skippy_vector[pt.id])}
  else{acti<- prepross.nan24to24HRS(acti_filenames[pt.id],
skippy_vector[pt.id])}
  sensor <- prepross.sensor(sensor_filenames[pt.id])
  aggy <- agg.time.dexluxe(sensor,acti)
  filterNITE <- FilterNightIndicies(aggy)
  filterNITE$id <- patient.id[pt.id]
  CompleteData<- rbind(CompleteData, filterNITE)
}

```

```

}

#get rid of variables I don't need
CompleteData$time.bin <- NULL
CompleteData$datetime.x <- NULL
CompleteData$New_time <- NULL
CompleteData$Line <- NULL
CompleteData$Date <- NULL
CompleteData$Time <- NULL
CompleteData$Marker <- NULL
CompleteData$Offwrist <- NULL
CompleteData$Activity <- NULL
CompleteData$Day <- NULL
CompleteData$whiteLight <- NULL
CompleteData$redLight <- NULL
CompleteData$greenLight <- NULL
CompleteData$blueLight <- NULL
CompleteData$IntervalStatus <- NULL
CompleteData$datetime.y <- NULL
CompleteData$New_time <- NULL

#re-naming columns
colnames(CompleteData) <- c("maxLUX", "maxMOVE", "maxSOUND", "SleepWake",
"Night", "Time", "ID")

#Exploration

group_by(CompleteData, ID) %>%
  summarise(nobs = n())

group_by(CompleteData, ID) %>%
  summarise(noches = max(Night))

# number of observations per person/night
table(CompleteData$ID, CompleteData$Night)

#Distinct # of Night across the sample
CompleteData %>% group_by(Night) %>% summarise(count = n_distinct(ID))

#removing 6th night
NoMore15Night6 <- CompleteData[CompleteData$Night!=6, ]

#Re-code the person with 0 nights of data
NoMore15Night6$Night[NoMore15Night6$ID==5]<- 1

NoMore15Night6 %>% group_by(Night) %>% summarise(count = n_distinct(ID))

# number of observations per person/night
table(NoMore15Night6$ID, NoMore15Night6$Night)

#Distinct # of Night across the sample
NoMore15Night6 %>% group_by(Night) %>% summarise(count = n_distinct(ID))

```

```

#Overwrite the code that had 6 nights
CompleteData <- NoMore15Night6

#CompleteData["GENDER"] <- NA #Female is 2, Male is 1
CompleteData$GENDER[CompleteData$ID==1] <- 2
CompleteData$GENDER[CompleteData$ID==2] <- 1
CompleteData$GENDER[CompleteData$ID==3] <- 2
CompleteData$GENDER[CompleteData$ID==4] <- 1
CompleteData$GENDER[CompleteData$ID==5] <- 1
CompleteData$GENDER[CompleteData$ID==6] <- 1
CompleteData$GENDER[CompleteData$ID==7] <- 1
CompleteData$GENDER[CompleteData$ID==8] <- 1
CompleteData$GENDER[CompleteData$ID==9] <- 1
CompleteData$GENDER[CompleteData$ID==10] <- 1
CompleteData$GENDER[CompleteData$ID==11] <- 1
CompleteData$GENDER[CompleteData$ID==13] <- 1
CompleteData$GENDER[CompleteData$ID==14] <- 1
CompleteData$GENDER[CompleteData$ID==15] <- 2
CompleteData$GENDER[CompleteData$ID==16] <- 1
CompleteData$GENDER[CompleteData$ID==18] <- 2
CompleteData$GENDER[CompleteData$ID==19] <- 1
CompleteData$GENDER[CompleteData$ID==20] <- 1

#CompleteData["GCS"] <- NA
CompleteData$GCS[CompleteData$ID==1] <- 14
CompleteData$GCS[CompleteData$ID==2] <- 7
CompleteData$GCS[CompleteData$ID==3] <- 15
CompleteData$GCS[CompleteData$ID==4] <- 9
CompleteData$GCS[CompleteData$ID==5] <- 14
CompleteData$GCS[CompleteData$ID==6] <- 15
CompleteData$GCS[CompleteData$ID==7] <- 15
CompleteData$GCS[CompleteData$ID==8] <- 15
CompleteData$GCS[CompleteData$ID==9] <- 3
CompleteData$GCS[CompleteData$ID==10] <- 3
CompleteData$GCS[CompleteData$ID==11] <- 15
CompleteData$GCS[CompleteData$ID==13] <- 15
CompleteData$GCS[CompleteData$ID==14] <- 14
CompleteData$GCS[CompleteData$ID==15] <- 15
CompleteData$GCS[CompleteData$ID==16] <- 14
CompleteData$GCS[CompleteData$ID==18] <- 14
CompleteData$GCS[CompleteData$ID==19] <- 14
CompleteData$GCS[CompleteData$ID==20] <- 15

#CompleteData["Race"] <- NA
# 1 = Black, 2= Hispanic, 3= Asian/Pacific Islander, 4 = White/Non-hispanic,
#5 = Other
CompleteData$Race[CompleteData$ID==1] <- 4
CompleteData$Race[CompleteData$ID==2] <- 4
CompleteData$Race[CompleteData$ID==3] <- 4
CompleteData$Race[CompleteData$ID==4] <- 4
CompleteData$Race[CompleteData$ID==5] <- 4

```

```

CompleteData$Race[CompleteData$ID==6] <- 4
CompleteData$Race[CompleteData$ID==7] <- 4
CompleteData$Race[CompleteData$ID==8] <- 2
CompleteData$Race[CompleteData$ID==9] <- 4
CompleteData$Race[CompleteData$ID==10] <- 4
CompleteData$Race[CompleteData$ID==11] <- 4
CompleteData$Race[CompleteData$ID==13] <- 4
CompleteData$Race[CompleteData$ID==14] <- 4
CompleteData$Race[CompleteData$ID==15] <- 4
CompleteData$Race[CompleteData$ID==16] <- 4
CompleteData$Race[CompleteData$ID==18] <- 4
CompleteData$Race[CompleteData$ID==19] <- 4
CompleteData$Race[CompleteData$ID==20] <- 4

#CompleteData["Age"] <- NA
CompleteData$Age[CompleteData$ID==1] <- 84
CompleteData$Age[CompleteData$ID==2] <- 34
CompleteData$Age[CompleteData$ID==3] <- 68
CompleteData$Age[CompleteData$ID==4] <- 58
CompleteData$Age[CompleteData$ID==5] <- 91
CompleteData$Age[CompleteData$ID==6] <- 31
CompleteData$Age[CompleteData$ID==7] <- 38
CompleteData$Age[CompleteData$ID==8] <- 70
CompleteData$Age[CompleteData$ID==9] <- 51
CompleteData$Age[CompleteData$ID==10] <- 78
CompleteData$Age[CompleteData$ID==11] <- 27
CompleteData$Age[CompleteData$ID==13] <- 34
CompleteData$Age[CompleteData$ID==14] <- 75
CompleteData$Age[CompleteData$ID==15] <- 78
CompleteData$Age[CompleteData$ID==16] <- 79
CompleteData$Age[CompleteData$ID==18] <- 79
CompleteData$Age[CompleteData$ID==19] <- 83
CompleteData$Age[CompleteData$ID==20] <- 85

write.csv(CompleteData, file = "ThirtysecDataAndDemographics.CSV")

#Functions to carry out BOOTSTRAP RESAMPLING FOR "standing" NON-AGG-DATA,
#as in, resampling the coefficients of NON-AGG-DATA as opposed to the
bootstrapped version if it...which is essentially a DIFFERENT data-set.

AnalysisofNonAggCoeff <- function(NonAggdata){
  mlm <- glmer(SleepWake ~ maxSOUND + maxLUX + maxMOVE + (1|ID/Night),
family = binomial,data = NonAggdata)
  MYCoeffs <- coefficients(summary(mlm))[-1,1] #this removes the
intercept values
  return(MYCoeffs)
}

Bootstrapline <- function(Nonaggdata){
  IDs <- unique(Nonaggdata$ID)
  newIDs <- sample(IDs, replace = TRUE)
  newdata <- NULL
  for(counter in 1:length(newIDs)){
    ind <- Nonaggdata$ID == newIDs[counter]

```

```

        newdata <- rbind(newdata, Nonaggdata[ind, ])
    }
    return(newdata)
}

BootStrapDistCoeff <- function(data, numsamp){
  stats <- NULL
  for( counter in 1:numsamp){
    resampdata <- Bootstrapline(data)
    resampstat <- AnalysisofNonAggCoeff(resampdata)
    stats <- rbind(stats, resampstat)}
  return(stats)
}

#Functions to Carry out BOOTSTRAP RESAMPLING FOR PREDICTED NON-AGG-DATA

AnalysisofNonAgg <- function(NonAggdata, dfSE){
  mlm <- glmer(SleepWake ~ maxSOUND + maxLUX + maxMOVE + (1|ID/Night),
family = binomial, data = NonAggdata)
  DataPredict <- predict(mlm, newdata = dfSE, type = "response", re.form
= NA)
  MYDifferences <- DataPredict[1] - DataPredict[2:4]
  return(MYDifferences)
}

Bootstrapline <- function(Nonaggdata){
  IDs <- unique(Nonaggdata$ID)
  newIDs <- sample(IDs, replace = TRUE)
  newdata <- NULL
  for(counter in 1:length(newIDs)){
    ind <- Nonaggdata$ID == newIDs[counter]
    newdata <- rbind(newdata, Nonaggdata[ind, ])
  }
  return(newdata)
}

BootStrapDist <- function(data, numsamp, dfSE){
  stats <- NULL
  for( counter in 1:numsamp){
    resampdata <- Bootstrapline(data)
    resampstat <- AnalysisofNonAgg(resampdata, dfSE)
    stats <- rbind(stats, resampstat)}
  return(stats)
}

#Functions to Carry out BOOTSTRAP RESAMPLING FOR PREDICTED NON-AGG-DATA

```

```

AnalysisofNonAgg <- function(NonAggdata, dfSE){
  mlm <- glmer(SleepWake ~ maxSOUND + maxLUX + maxMOVE + (1|ID/Night),
family = binomial,data = NonAggdata)
  DataPredict <- predict(mlm, newdata = dfSE, type = "response",re.form
= NA)
  MYDifferences <- DataPredict[1] - DataPredict[2:4]
  return(MYDifferences)
}

Bootstrapline <- function(Nonaggdata){
  IDs <- unique(Nonaggdata$ID)
  newIDs <- sample(IDs, replace = TRUE)
  newdata <- NULL
  for(counter in 1:length(newIDs)){
    ind <- Nonaggdata$ID == newIDs[counter]
    newdata <- rbind(newdata, Nonaggdata[ind, ])
  }
  return(newdata)
}

BootStrapDist <- function(data, numsamp, dfSE){
  stats <- NULL
  for( counter in 1:numsamp){
    resampdata <- Bootstrapline(data)
    resampstat <- AnalysisofNonAgg(resampdata, dfSE)
    stats <- rbind(stats, resampstat)}
  return(stats)
}

```{r}
calculateConfIntv <- function(CoverageProbability, ResampCoeff){
 tails <- 1 - CoverageProbability
 halfTails <- tails/2
 bigTails <- 1- halfTails
 PostConfIntv <- quantile(ResampCoeff, c(halfTails, bigTails))
 return(PostConfIntv)
}
```

```{r}
a <- seq(0.51, 1.0, by = 0.005)
head(a, n = 5)

```

```{r}
AnswerBox <- NULL

for(i in 1:length(a)){
 Result1 <- calculateConfIntv(a[i], TestBootStrapDistCoeff[,1])
}

```

```

 Result2 <- calculateConfIntv(a[i], TestBootStrapDistCoeff[,2])
 Result3 <- calculateConfIntv(a[i], TestBootStrapDistCoeff[,3])
 AllResults <- c(a[i], Result1, Result2, Result3)
 AnswerBox <- rbind(AnswerBox, AllResults)
 }
 ...

  ```{r}
  rm(list = ls())
  setwd("C:/Users/Ellita/Documents/Analysis")
  getwd()
  ...

  ```{r}
 #Now, you can analyze....
 TestBootDistIntro <- read.csv("TestBootOUTPUT.csv", header = TRUE)

 TestBootDist <- TestBootDistIntro[, -c(1)]

 colnames(TestBootDist)<- c("Sound", "Light", "Motion")
 ...

  ```{r}
  hist(TestBootDist[, 1])
  quantile(TestBootDist[, 1], c(0.025, 0.975))
  ...

  ```{r}

 hist(TestBootDist[, 2])
 quantile(TestBootDist[, 2], c(0.025, 0.975))
 ...

  ```{r}
  hist(TestBootDist[, 3])
  quantile(TestBootDist[, 3], c(0.025, 0.975))

  ...

  ```{r}
 rm(list = ls())
 ...

  ```{r}
  library("dplyr")
  library("lubridate")
  library("lme4")
  library("MASS")
  library("arm")
  library("Hmisc")
  library("psych")
  ...

  ```{r}
 setwd("C:/Users/Ellita/Documents/Analysis")

```

```

NonAggdata <-read.csv(file = "NonAggdata.csv", header = TRUE)
```

```{r}
NonAggdata $X <- NULL
```

```{r}
head(NonAggdata , n = 5)
str(NonAggdata)
names(NonAggdata)
dim(NonAggdata)
```

```{r}
#The number of observations per subject
group_by(NonAggdata , ID) %>%
 summarise(nobs = n())
```

```{r}
#The number of nights per subject
group_by(NonAggdata , ID) %>%
 summarise(noche = max(Night))
```

```{r}
#Number of observations per subject/night
table(NonAggdata $ID, NonAggdata $Night)
```

```{r}
#Distinct number of nights across the sample
NonAggdata %>% group_by(Night) %>% summarise(count = n_distinct(ID))
AvgNight <- NonAggdata %>% group_by(Night) %>% summarise(count =
n_distinct(ID))
```

```{r}
#Histograms of predictor variables and counfounding variables
hist(NonAggdata $maxSOUND)
hist(NonAggdata $maxLUX)
hist(NonAggdata $maxMOVE)
hist(NonAggdata$Age)
hist(NonAggdata$GCS)
```

```{r}
table(NonAggdata$SleepWake)
mean(NonAggdata$SleepWake)
65058 = 0; 20601 = 1 ; total number of 1's / observations = 0.2405 or 24%
#subjects in this sample were awake for 24% of the time per each night.

```

```

....

```{r}
#standardized sound, light, and motion were omitted because they would not
reflect true values of decibels, lumens, and proportions, respectivley.
describe(NonAggdata[c("maxLUX","maxMOVE", "maxSOUND", "Night", "GCS",
"Age")])
```

```{r}
#standardized sound, light, and motion were omitted because they would not
reflect true values of decibels, lumens, and proportions, respectivley.
df <- as.data.frame(NonAggdata[c("maxLUX","maxMOVE", "maxSOUND", "Night",
"GCS", "Age")])
print(corr.test(df, method = "pearson"), short = FALSE)
```

* Before Running our random effects model, let's first see if there is an
association between the variables with an ordinary least squares (OLS) model.
We anticipate there will be an association, but we won't use this mdoel to
make our final decision on the strength of associations because OLS *over
simplifies* the associations of our observations.
```{r}
#Unscaled "environmental" variables
OLS.M0 <- glm(SleepWake ~ maxSOUND + maxLUX + maxMOVE, data = NonAggdata,
family = binomial())
summary(OLS.M0)
```

```{r}
#Unscaled "environmental" variables + Age
OLS.M0_Age <- glm(SleepWake ~ maxSOUND + maxLUX + maxMOVE + Age, data =
NonAggdata, family = binomial())
summary(OLS.M0_Age)
```

```{r}
#Unscaled "environmental" variables + GCS
OLS.M0_GCS <- glm(SleepWake ~ maxSOUND + maxLUX + maxMOVE + GCS, data =
NonAggdata, family = binomial())
summary(OLS.M0_GCS)
```

```{r}
#Unscaled "environmental" variables + Age + GCS
OLS.M0_AgeGcs <- glm(SleepWake ~ maxSOUND + maxLUX + maxMOVE + Age + GCS,
data = NonAggdata, family = binomial())
summary(OLS.M0_AgeGcs)
```

```

\* Now, we have to try our multi-level model. We will begin with models that include only the outcome variable and the random effect.

```

```{r}
mlm.M0 <- glmer(SleepWake ~ (1|ID), family = binomial, data = NonAggdata )
BIC(mlm.M0)
summary(mlm.M0)
```

```

```

```{r}
mlm.M1 <- glmer(SleepWake ~ (1|Night) + (1|ID), family = binomial, data =
NonAggdata )
BIC(mlm.M1)
summary(mlm.M1)
```

```

```

```{r}
mlm.M2 <- glmer(SleepWake ~ (1|Night) + (1|ID) + (1|ID:Night), family =
binomial, data = NonAggdata )
BIC(mlm.M2)
summary(mlm.M2)
```

```

```

```{r}
mlm.M3 <- glmer(SleepWake ~ (1|ID/Night), family = binomial, data =
NonAggdata)
BIC(mlm.M3)
summary(mlm.M3)
```

```

\* It seems that including "ID" and "Night" as a variable to group by is beneficial as evidenced by a decrease in the BIC. We should therefore use the "Night" to group "ID"'s. The current abbreviation "(1|ID/Night)" does the following:  $(1|ID) + (1|ID : Night)$ . This positions the first part of this formula as ID having it's own random intercept while the second part of this equation is the product between ID and NIGHT. This effectively "levels" the influences/variability in the patients and the variability in the Nights they are housed on the unit.

```

```{r}
SOUNDonly_mlm.M0 <- glmer(SleepWake ~ Scale.maxSOUND + (1|ID/Night),family =
binomial, data = NonAggdata)
BIC(SOUNDonly_mlm.M0)
summary(SOUNDonly_mlm.M0)
```

```

```

```{r}
LUXonly_mlm.M0 <- glmer(SleepWake ~ Scale.maxLUX + (1|ID/Night), family =
binomial, data = NonAggdata)
BIC(LUXonly_mlm.M0)
summary(LUXonly_mlm.M0)
```

```

```

```{r}
MOVEonly_mlm.M0 <- glmer(SleepWake ~ Scale.maxMOVE + (1|ID/Night), family =
binomial, data = NonAggdata)

```

```

BIC(MOVEonly_mlm.M0)
summary(MOVEonly_mlm.M0)
```

```{r}
#From these single-fixed effects models, we see the best BICs are:
#motion (BIC = 77069.88)
#then sound (BIC = 80,079)
#then light (BIC = 82,080)

#Now we will add each variable sequentially to build the model.
```

```{r}
mlm.SoundMove <- glmer(SleepWake ~ Scale.maxSOUND + Scale.maxMOVE +
(1|ID/Night), family = binomial, data = NonAggdata)
BIC(mlm.SoundMove)
summary(mlm.SoundMove)
```

```{r}
mlm.SoundLight <- glmer(SleepWake ~ Scale.maxSOUND + Scale.maxLUX +
(1|ID/Night), family = binomial, data = NonAggdata)
BIC(mlm.SoundLight)
summary(mlm.SoundLight)
```

```{r}
mlm.LightMove <- glmer(SleepWake ~ Scale.maxLUX + Scale.maxMOVE +
(1|ID/Night), family = binomial, data = NonAggdata)
BIC(mlm.LightMove)
summary(mlm.LightMove)
```

```{r}
mlm.SoundLightMove <- glmer(SleepWake ~ Scale.maxSOUND + Scale.maxLUX +
Scale.maxMOVE + (1|ID/Night), family = binomial, data = NonAggdata)
BIC(mlm.SoundLightMove)
summary(mlm.SoundLightMove)
```

```{r}
mlm <- glmer(SleepWake ~ maxSOUND + maxLUX + maxMOVE + (1|ID/Night), family
= binomial, data = NonAggdata)
BIC(mlm)
summary(mlm)
```

```{r}
mlm.SoundLightMoveAge <- glmer(SleepWake ~ Scale.maxSOUND + Scale.maxLUX +
Scale.maxMOVE + Age + (1|ID/Night), family = binomial, data = NonAggdata)
BIC(mlm.SoundLightMoveAge)

```

```
summary(mlm.SoundLightMoveAge)
```

```{r}
mlm.SoundLightMoveGCS <- glmer(SleepWake ~ Scale.maxSOUND + Scale.maxLUX +
Scale.maxMOVE + GCS + (1|ID/Night), family = binomial, data = NonAggdata)
BIC(mlm.SoundLightMoveGCS)
summary(mlm.SoundLightMoveGCS)
```

###GCS or Age, did not improve the model. In the end, the best combo, based
on BIC, is sound, light, and motion (BIC = 76, 578). We will go from there to
get our predicted probability.
###This concludes the script for model selection.###
```