A Pilot Study to Determine the Consistency of Simultaneous Sleep Actigraphy Measurements Comparing All Four Limbs of Patients with Parkinson Disease

by

Vineet Prasad

A thesis submitted in partial fulfillment of the requirements for the degree of

Master of Science

in
Rehabilitation Science

Faculty of Rehabilitation Medicine
University of Alberta

Abstract

Background: Wrist actigraphy is a form of objective sleep measurement that has gained a central role in research and clinical settings. Although actigraph data is available for sleep disorders concerning medical and neurobehavioral disorders, the literature identifies that sensitivity of actigraph data in studies of persons with Parkinson disease (PD) are not robust. Guidelines for actigraphy recommend placing the monitor on the non-dominant wrist. However, this potentially can be the most involved limb for someone with PD, and so alternative placement would be preferred. To date, there are few studies on sleep actigraphy use for adults with PD, and specifically, no research to explore the degree of variability in actigraph findings when comparing simultaneous readings from all four limbs (upper/lower, dominant/non-dominant limb).

Aim: This study aimed to determine the degree of sleep actigraph score variation in persons with PD when actigraph placed simultaneously on all four limbs.

Methods: Four participants were recruited through the University of Alberta Faculty of Rehabilitation student-lead teaching clinics and wore a sleep actigraph (Actigraph Wgt3X-BT) on each limb for seven nights. The within-participant data from the four actigraphs were compared to determine the degree of consistency.

Results: We found that all participants' sleep efficiency (SE) and total sleep time (TST) scores were higher in the lower limb than upper limb. There was no notable difference seen in sleep variables between the dominant and non- dominant arm.

Conclusion: We concluded that simultaneous actigraphy measurement did not show notable variation between dominant and non-dominant arms. However, a discrepancy was seen between upper and lower limbs actigraph scores. Further study is warranted to develop guidelines for sleep actigraphy use in this population.

Preface

This thesis is an original work done by Vineet Prasad under the supervision of Dr. Cary A Brown. The research project, of which this thesis is a part, was published as "Prasad, V., & Brown, C. (2017). A Pilot Study to Determine the Consistency of Simultaneous Sleep Actigraphy Measurements Comparing All Four Limbs of Patients with Parkinson Disease. *Geriatrics*, *3*(1), 1. MDPI AG. Retrieved from http://dx.doi.org/10.3390/geriatrics3010001". The manuscript of the published paper is attached in the Appendix III (pg-50).

Acknowledgment

My first sincere gratitude to my supervisor Dr. Cary A Brown who provided me the opportunity to grow and supported me throughout the course with her guidance, motivation and above all patience. I could not have done this project without her support and guidance. I would also like to thank the rest of my committee: Associate Professor. Teresa Paslawski and Professor. Shaniff Esmail, for their valuable time, constructive feedback, and assistance during the study. I would also like to acknowledge my participants who volunteered for the project.

Lastly, I would like to thank my better-half and my family who stood by me in every decision.

Table of Contents

List of Tables

Chapter1. Introduction

1.1 Problem statement

Evidence from the literature suggests that 50% to 70 % of persons with PD have some form of sleep disorders (Selvaraj & Keshavamurthy, 2016). There are many clinical scales for the assessment of sleep disorders in persons with PD; however, these scales may not adequately and quantitatively reflect the disease severity and efficacy of treatment before and after a trial in a research setup. Many of the evaluative measures are subjective or vulnerable to recall bias (Högl et al., 2010). Wrist actigraphy has gained a central role as an objective assessment tool in sleep research and clinical settings (Sadeh, 2011). Research shows that actigraphy is sensitive in the evaluation of unique sleep patterns associated with sleep disorders as well as with other medical or neurobehavioral disorders (Ancoli-Israel et al., 2003; Sadeh, 2011). Furthermore, actigraphy is also sensitive in detecting sleep changes associated with drug treatments and non-pharmacologic interventions (Ancoli-Israel et al., 2003; Sadeh, 2011). Compared to overnight polysomnography (PSG) study for the assessment of sleep, actigraphy offers several advantages that have made it appealing to researchers and clinicians. Studies have reported actigraphy to be more feasible for use over extended periods of time (i.e., days to weeks), hence allowing the collection of data about day to day variability in sleep patterns (Sadeh, 2011). Further, actigraphy provides information about sleep and wake patterns in the patient's natural sleep environment (Maglione et al., 2013; Stavitsky, Saurman, McNamara, & Cronin-Golomb, 2010). Although validated research data about actigraphy is available for sleep disorders concerning medical or neurobehavioral disorders, there is still lack of data related to the sensitivity of actigraphy usage in neurological conditions such as PD. Persons with PD suffer from motor disorder (i.e., tremors, bradykinesia) along with sleep dysfunction and these symptoms may lead to a biased assessment

of sleep patterns. The literature recommends placement of the actigraph on the non-dominant wrist for collecting sleep variable. However, this potentially might be the most affected limb for a person with PD. Hence there is a need to augment the evidence concerning placement of actigraph in person with PD and to explore the degree of variability in actigraph findings when comparing simultaneous readings from all four limbs (upper/lower, dominant/non-dominant limb).

1.2 Study objective

The objective of this study was to determine the consistency of actigraph readings in measuring sleep patterns when placed simultaneously along four limbs in person with Parkinson disease.

Chapter2. Literature review

This chapter gives a brief introduction to PD and common sleep problems seen in persons with PD. Furthermore, this chapter identifies and describes the various subjective and objective tools used for sleep assessment in people with PD. Subsequently, the chapter discusses advantages and disadvantages of various subjective and objective sleep assessment tools. Finally, this chapter illuminates specifically the use of actigraphy as an objective tool and its advantages in relation to other assessment tools (both subjective and objective) in research and clinical practice.

2.1 Parkinson disease

Parkinson disease is the second most common neurodegenerative disease after Alzheimer's disease, and it was first explained by James Parkinson in his book "Essay on the Shaking Palsy" (Olanow, Lang, & Stocchi, 2011). Etiology of the disease is not yet known, but in most cases, it appears idiopathic. Idiopathic PD has been proposed to be the interaction between environmental factors and genetic factors (Chin-Chan, Navarro-Yepes, & Quintanilla-Vega, 2015). Epidemiological data, over the recent years, have shown a rise in the prevalence of patients with PD (The Government of Canada, 2014). National population health study of neurological conditions, led by the Public Health Agency of Canada and the Neurological Health Charities, Canada (2014) has stated that the number of prevalent cases of PD by the year 2021 would be 116,800 compared to 84,700 observed cases in the year 2011. Additionally, the study indicated that by the year 2031 number of people living with PD would be 148,800 compared to 71,500 in the year 2011.

There are mainly two groups of symptoms, "motor" and "non-motor," that characterize PD. Motor manifestation of PD is due to abnormality of the motor system of the Central Nervous

System (CNS), and non-motor symptoms occur either as a result of the adverse effect of drug treatment or due to changes which take place in the different organ systems, such as endocrine, respiratory, and digestive system of the body (Sveinbjornsdottir, 2016).

The cardinal motor features of PD start to appear when approximately up to 80% of dopaminergic cells in the nigrostriatal pathway are lost (Chung et al. 2001). The cardinal motor features include symptoms such as rigidity, bradykinesia, postural instability, and tremors.

In addition to motor symptoms, a wide range of non-motor symptom occurs in PD. Commonly seen non-motor symptoms include disturbances in autonomic function, sleep disturbances, cognitive and psychiatric disturbances (Sveinbjornsdottir, 2016). Some of the non–motor symptoms manifest before the onset of motor symptoms (Visanji & Marras, 2015). Non-motor symptoms may start as early as 10 or more years before diagnosis (Schrag et al. 2015), and presentation with non-motor symptoms may delay diagnosis (O'Sullivan et al. 2008). Following the provocative observation that changes in regulation of the sleep and wakefulness cycle may occur years before the onset of PD motor symptoms, sleep disorders have become the primary focus as a preclinical marker of the eventual onset of PD (Elbaz, 2016; Lugaresi & Provini, 2001; Mahlknecht, Seppi, & Poewe, 2015).

2.2 Sleep disorders in Parkinson disease

Sleep is the periodic reversible physiological state of loss of consciousness from which arousal of a person is possible by adequate sensory stimuli (Selvaraj & Keshavamurthy, 2016). Sleep disorders are common in persons with PD, and these come under the non-motor component of PD (Selvaraj & Keshavamurthy, 2016). Sleep disorders affect 60% to 90% of persons with PD

(Jahan, Hauser, Sullivan, Miller, & Zesiewicz, 2009; Kumar, Bhatia, & Behari, 2002; Selvaraj & Keshavamurthy, 2016). A study conducted by Selvaraj and Keshavamurthy (2016), reported that more than 70% of persons with PD experienced disturbed sleep.

The most common sleep disorders for persons with PD are insomnia, abnormal sleep behaviors suggesting rapid eye movement behavioral disorder, excessive daytime sleepiness (EDS) and restless leg syndrome (RLS) (Peralta et al., 2009; Sveinbjornsdottir, 2016). The motor and non-motor consequences of PD can hinder the initiation, continuity, and maintenance of sleep (Jahan et al., 2009). These consequences include difficulty turning over or moving in bed, pain, tremor, rigidity, slowness of movement, cramps, morning dystonia, and the coexistence of depression, anxiety, cognitive impairment, and neural loss of the regulatory sleep centers in the brainstem and thalamocortical pathways (dos Santos, Kohlmeier, & Barreto, 2015; Kummer & Teixeira, 2009).

Sleep restrictions due to sleep disorders can cause significant neurobehavioral deficits and physiological changes in persons with PD (Selvaraj & Keshavamurthy, 2016). Studies on sleep restrictions in healthy adults have shown that significant cognitive dysfunction (i.e., reduced vigilant attention and working memory) can occur if sleep is continuously restricted to less than 7 hours per night (Banks & Dinges, 2007; Lowe, Safati, & Hall, 2017). In addition, long-term sleep restriction can be a risk factor for obesity, cardiovascular morbidity, traffic accidents and death (Banks & Dinges, 2007). Considering the fact that over two-thirds of persons with PD have sleep disorders at some stage of the disease, and that their total sleep time decreases with increasing disease severity (Selvaraj & Keshavamurthy, 2016), long-term sleep restrictions can lead to profound changes in neurobehavioral and physiological functions of persons with PD (Banks & Dinges, 2007). Also, with so many subtypes of sleep disorders seen in PD and the fact

that some sleep disorders can occur ten years prior to the onset of motor symptoms, it becomes necessary to detect the sleep problems in PD. Detection of sleep problems requires both subjective and objective assessment tools.

2.3 Assessment of sleep problems in Parkinson disease

This section will review sleep assessment tools for persons with PD. Assessment of sleep disorders in persons with PD is based on clinical history, caregiver reports, questionnaires, sleep logs, and polysomnography or video recordings (Margis et al., 2009). Assessment may be carried out subjectively with self-reported measures, e.g., rating scales, questionnaires (Högl et al., 2010) or objectively, e.g., polysomnography (PSG) (Tolleson, Bagai, Walters, & Davis, 2016), multiple sleep latency test (MSLT) (Ataide, Franco, & Lins, 2014; Zea-Sevilla & Martínez-Martín, 2014), and actigraphy.

Self-reported measures provide a feasible and economical way of assessment that also captures the subjective view about sleep of persons with PD. The Movement Disorder Society (MDS) has recommended two specific and two generic psychometrically tested scales for use in PD research (Högl et al., 2010; Zea-Sevilla & Martínez-Martín, 2014).

The two specific scales recommended by the MDS are the Parkinson's disease sleep scale (PDSS) (Högl et al., 2010) and Scales for Outcome in PD- Sleep (SCOPA – Sleep) (Högl et al., 2010).

1.) Parkinson's Disease Sleep Scale (PDSS).

The PDSS determines the nocturnal problems disturbing sleep in persons with PD over the previous week (Högl et al., 2010; Zea-Sevilla & Martínez-Martín, 2014). The scale contains 15 items formulated as questions and focused on nocturnal sleep (Zea-Sevilla & Martínez-Martín, 2014). A study done by Martinez-Martin et al., (2008) suggested that PDSS can be used for obtaining a profile of potential causes of "bad sleep" but is barely useful to assess daytime sleepiness. In a study done by Muntean et al., (2016), PDSS-2 showed a sensitivity of 77.6% and a specificity of 74.3% in relation to physician's evaluation of PD-specific sleep problem.

2.) Scales for Outcomes in PD-Sleep (SCOPA-S).

The SCOPA-S is a short, self-reported tool for Parkinson sleep disorders research. There are three components; a nighttime scale, a single item about the perceived quality of nocturnal sleep, and a daytime sleepiness scale (Zea-Sevilla & Martínez-Martín, 2014). A study done by Martinez-Martin et al., (2008), showed that as compared to PDSS (which is not helpful in assessment of daytime sleepiness), the SCOPA-S assesses both nocturnal sleep disorders and daytime somnolence and so has an advantage over the PDSS. A study by Marinus et al., (2003) found that SCOPA-S is highly reliable with an internal consistency of .88 and .91 (Cronbach α) for nighttime sleep and daytime sleepiness scales respectively.

Additionally, two recommended generic scales by MDS are the Pittsburgh Sleep Quality Index (PSQI) (Högl et al., 2010) and Epworth sleepiness scale (ESS) (Högl et al., 2010).

3.) Pittsburgh Sleep Quality Index (PSQI).

The PSQI is a self- rating questionnaire designed to evaluate sleep quality and to examine sleep habits and disturbance during the previous month (Högl et al., 2010). It consists of 19 items that

produce an estimate of global sleep quality based on the following seven components: perceived sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, hypnotic medication use, and daytime dysfunction (Takács et al., 2016). A study conducted by Takács et al., (2016) with a Hungarian population found the internal consistency of PSQI, as measured by Cronbach's alpha, to be 0.79 (Takács et al., 2016). Furthermore, the study found the PSQI to be a reliable, valid, and standardized measure for the assessment of subjective sleep quality in clinical and research settings.

4.) Epworth Sleepiness Scale (ESS).

The ESS is a subjective measure used to assess daytime sleepiness in persons with PD. It is a self -rating scale consisting of eight items that assess the tendency to doze in specific situations. It has shown excellent psychometric properties for presence and severity of daytime sleepiness in both healthy subjects and those with primary sleep disorders, such as sleep apnea (Högl et al., 2010). For PD, the ESS has been psychometrically tested (Knie, Mitra, Logishetty, & Chaudhuri, 2011). According to Högl et al., (2010), ESS is suitable for screening for sleepiness but unsuitable for screening for episodes of sudden sleep onset in persons with PD.

Moving on, literature congruently illustrates the application of neurophysiological sleep assessment tools such as MSLT and PSG to obtain a quantified measurement of daytime sleepiness or overall sleep structure in persons with PD (Högl et al., 2010).

1) Multiple Sleep Latency Test (MSLT).

The MSLT is an objective tool used for assessment of patients suspected with idiopathic hypersomnia (Ataide et al., 2014). The MSLT involves a series of naps in a sleep-inducing

environment, with an interval of 2 hours between them. The data collected, in the form of sleep latency values, is interpreted by a sleep clinician. For example, a sleep latency of less than 5 minutes indicates a considerable risk of impairment regarding performed task and can be associated with a pathological level of daytime sleepiness (Ataide et al., 2014; Shpirer et al., 2007). The MSLT can be used to assess a person with PD suffering from pathological sleepiness, such as narcolepsy and idiopathic hypersomnia and sleep-onset REM periods (Ataide et al., 2014).

2) Polysomnography (PSG).

Polysomnography is considered a gold standard tool for assessment of sleep-related problems. PSG is a multichannel measurement system administered overnight in a hospital-based setup to generate polysomnographic reports (Sadeh, 2011). Polysomnographic reports routinely include sleep, electrocardiogram, respiratory, and periodic leg movement data (Kushida et al., 2005). Polysomnography is frequently conducted over a three night period with the first night's results being discarded (Tryon, 2004).

2.4 Challenges in the assessment of sleep disorders in persons with PD

The multifactorial and multidimensional nature of sleep disorders in PD precludes the use of a single assessment tool for evaluation. Evaluation of sleep in PD can be done through history taking and standardized self-report scales (sometimes considered as subjective tools), or by use of neurophysiological methods (sometimes referred as objective tools) such as the use of PSG or MSLT. However, there are many challenges involving the use of both subjective and objective tools.

Objective tools such as PSG and MSLT need a hospital-based setting and are costly and time-consuming. Polysomnography requires several nights of sleep in a sleep lab, and contributes to patient burden and cost of the research (Stavitsky et al., 2010). Furthermore, implementation of objective tools does not take place in the patient's natural sleep environment and is done overnight in clinical settings which might alter a patient's typical sleep patterns (i.e., scheduled bedtime and wake-up time) (Ancoli-Israel et al., 2003; Sadeh, 2011).

Subjective tools, on the other hand, are more realistic as they reflect real-life situations and provide valuable information for evaluating symptoms severity (Högl et al., 2010). Also, subjective tools are relatively simple and easy to apply, and they provide comprehensive information at a low cost (Högl et al., 2010; Zea-Sevilla & Martínez-Martín, 2014). Hence, they are commonly used in clinical research and practice (Zea-Sevilla & Martínez-Martín, 2014). However, in some situations, self- reports are insufficient. For example, the terms used in a subjective tool might be obscure and can be influenced by psychological factors such as anxiety, depression, and somatization (Stavitsky et al., 2010). Results of self-reported sleep scales can be biased due to recall problems, medications, and the occurrence of motor symptoms in PD (Högl et al., 2010). Also, consideration should be given to the phenomenon of sleep state misperception which refers to a person thinking he or she has been awake all night, but the bed partner (or objective PSG) confirms the contrary (Högl et al., 2010). Hence, in combination with self- report sleep measures, practical, cost-effective and less cumbersome tools such as actigraphs are needed to screen for sleep disturbance and daytime sleepiness in PD patients.

To conclude, there are various sleep scales and objective tools to assess sleep problems in persons with PD. However, these assessment tools have limitations. For e.g., as mentioned earlier subjective tools such as PDSS is "barely useful" for measuring daytime sleepiness.

Moreover, subjective tools such as PDSS, ESS can yield biased results due to recall problems and sleep state misperception. Also, in the circumstances where cognitive abilities of the patient are compromised, administration of subjective tools can become a challenging task for a researcher.

Moving on, objective tools such as PSG and MSLT are sophisticated and can be only used in hospital settings, which increases the cost of burden on the patients and families. Since, these tools are employed in hospital settings; it potentially can interfere with patients' natural sleep environment (Sadeh, 2011). Thus, there is a need for an alternate assessment tool which is cost-effective, has good reliability , less intricate and can be employed in the natural sleep environment of a person such as an actigraph (Zinkhan et al., 2014). The following section will present a detail explanation about actigraph.

2.5 Actigraph

In recent years, there has been an increasing amount of literature on the use of actigraphy. Actigraphy has gained a central role as an objective assessment tool in sleep medicine and research (Ancoli-Israel et al., 2003; Prasad & Brown, 2017; Sadeh, 2011). An actigraph is a small wrist-watch like device which can be placed on the body's appendages (wrist, shoulder, trunk, hip, and ankle) to record motion (Ancoli-Israel et al., 2003; Prasad & Brown, 2017; Sadeh, 2011). The information about activity/ inactivity is downloaded and analyzed using a specific algorithm to estimate wake / sleep (Ancoli-Israel et al., 2003; Sadeh, 2011). There are many commercially available variations of actigraphs. The actigraphs available use different algorithms and methodologies and have dissimilarity in regard to the detection and recording of

movements (Ancoli-Israel et al., 2003; Sadeh, 2011; Tryon, 2004). A band-pass filter is commonly used to capture the movement. The accuracy of accelerometers is highly dependent on the sensitivity and specificity of the band-pass filter (Sadeh, 2011; Tryon, 2004; Wallén, Nero, Franzén, & Hagströmer, 2014). Literature recommends the use of .25 to 2-3 Hz band-pass filter which eliminates languid movements of less than .25 Hz and movements faster than 2-3 Hz (Ancoli-Israel et al., 2003; Wallén et al., 2014). This recommendation is based on evidence that normal voluntary human movement does not exceed beyond 3-4 Hz (Ancoli-Israel et al., 2003; Calogiuri, Weydahl, & Carandente, 2011). However, there is an inconsistency with this argument. Some evidence suggests the use of .5-11 Hz as it is supposed to reduce the gravitational artifact while capturing some faster movement occurring in younger participants (Ancoli-Israel et al., 2003). The motion captured is usually transduced and stored in digitized form. Some aspect of transduction depends upon the program used by the researcher. While other aspects of digitizing are inbuilt and may rely on the vendors (Ancoli-Israel et al., 2003; Sadeh, 2011). One key component is how the information is digitized: time above threshold, zero crossings or digital integration (Ancoli-Israel et al., 2003; Sadeh, 2011). Some research has shown the advantages of using digital integration over the other forms of digitizing (Sadeh, 2011). Digital integration involves sampling the accelerometry output signal at a high rate, then calculating the area under the curve for each epoch (Ancoli-Israel et al., 2003; Sadeh, 2011). As explained earlier, actigraphy is not a unitary methodology. Multiple vendors offer a range of actigraphs with different operating characteristics (Mantua, Gravel, & Spencer, 2016; Sadeh, 2011; Tryon, 2004). Nevertheless, the design of the actigraph and program should be selected according to the population evaluated (Maglione et al., 2013; Sadeh, 2011; Zinkhan et al., 2014).

Most of the studies to validate and establish evidence for the use of actigraphy have compared actigraphy to either PSG or sleep diaries or both (Chen et al., 2015; Sadeh, 2011; Zinkhan et al., 2014). A procedural difficulty in doing so is that actigraphy is a single-channel measurement system, whereas PSG is a multichannel measurement system (Tryon, 2004). Hence it will be impossible for actigraphy to duplicate PSG. Furthermore, it is difficult to accurately time-lock the epochs of the actigraph with those of PSG (Sadeh, 2011). A study done by Samson et al.,(2016) concluded that with the appropriately designated parameters for a nap/wake-bout diagnostics, actigraphy could be used for detecting segmented sleep. Recent literature supports the use of actigraphy in detecting the sleep patterns associated with specific sleep disorders, medical or neurobehavioral disorders, pharmacological and non-pharmacological interventions (Sadeh, 2011).

Besides sleep disorders, actigraphy is found to be useful in other population where PSG might be challenging to obtain (Ancoli-Israel et al., 2003; Sadeh, 2011). A study done by Latshang et al., (2016) found actigraphy is valuable for assessing effects of altitude and other environmental influences on sleep for an extended period in altitude travelers. Furthermore, a study done by Melegari et al., (2016) used actigraphy in preschoolers with attention deficit hyperactivity disorder (ADHD) to show the increased motor activity during sleep and night-to-night variability for sleep duration and motor activity. Also, reliability and validity studies in healthy adults have demonstrated that actigraphy is highly correlated with polysomnography for differentiating sleep from wake states (Sadeh, 2011; Stavitsky et al., 2010).

Few studies have demonstrated the usefulness of actigraphy in measuring sleep parameters in persons with PD (Kotschet et al., 2014; Maglione et al., 2013; Pan et al., 2013; Ray et al., 2014; Stavitsky et al., 2010). A study done by Maglione et al.(2013), revealed that actigraphy might be

used for measurement of mean total sleep time (TST), sleep efficiency (SE), and wake after sleep onset (WASO) values in groups of patients with mild to moderate PD. A study done by Stavitsky et al., (2010) showed the strong correlation of subjective sleep measures with actigraphy-derived estimates of sleep quality and suggested the use of actigraphy together with subjective tools such as PDSS, SCOPA-S for assessment of sleep quality in persons with PD.

When compared to overnight PSG, actigraphy is more feasible for use over extended periods of time (.i.e. days to weeks), thereby allowing for the collection of information about day to day variability in sleep patterns (Maglione et al., 2013; Stavitsky et al., 2010). Further, actigraphs are typically used at home and therefore provide objective information about sleep and wake patterns in the patient's natural sleep environment (Maglione et al., 2013; Stavitsky et al., 2010).

However, there are some drawbacks regarding the use of actigraphy in persons with PD. The actigraph is sensitive to small movements, and this might make the use of actigraphy difficult in persons with PD suffering from moment-to-moment motor fluctuations (e.g., medication off time), tremors and dyskinesia (Pan et al., 2013). Data derivation from actigraph is based on the self-report of sleep and wake up time on a sleep diary. However, use of a sleep diary to gain the time of sleep and awakening might be biased due to sleep-state misperception, which might lead to false scores of the data collected (Sadeh, 2011). Moreover, the manufacturer's default scoring parameter may not provide the best data when using actigraphy in persons with PD (Maglione et al., 2013; Wallén et al., 2014). Furthermore, as mentioned earlier, the score settings depend on multiple factors including the sleep measure of interest to the investigator or clinician, the device being used and the population being assessed (Maglione et al., 2013; Wallén et al., 2014). Also, there are issues regarding placement of the actigraph.

Available literature shows differences in data when the actigraphs are placed on different sites such as the ankle, hip, or wrist (Hislop, Palmer, Anand, & Aldin, 2016; Ray et al., 2014; Slater et al., 2015; Zinkhan et al., 2014). The data available from studies on other populations suggest that the wrist, in general, is more accurate for sleep estimation than other placements (Hislop et al., 2016; Slater et al., 2015; Zinkhan et al., 2014). A study done by Hislop, Palmer, Anand, & Aldin, (2016) investigated agreement between actigraph estimates of physical activity intensity and sedentary behavior when comparing wrist-worn to hip-worn actigraph accelerometers in preschool children during free-play. They found that total vector magnitude (VM) count output and the mean VM count per minute data collected from wrist and the hip were significantly correlated ($p < 0.01$). However, in the same study, a notable and systematic difference with wide limits of agreement, was found between hip and wrist data. A study done by Slater et al.,(2015) simultaneously measured sleep using wrist actigraphy, hip actigraphy, and PSG and found that the wrist actigraph scored sleep with reasonable specificity while hip actigraph sleep scores had unacceptably low specificity. To date, the relationship between placement sites and sleep parameters in persons with PD is inconclusive, and further research is warranted.

In summary, although studies have demonstrated the potential usefulness of actigraphy in measuring sleep parameters in persons with PD (Maglione et al., 2013; Stavitsky et al., 2010), there is a lack of clear, evidence-based direction regarding monitor placement (Hislop et al., 2016; Ray et al., 2014). The data available from studies of other patient populations suggest that the wrist, in general, is more accurate for sleep variable estimation than other placement sites (Hislop et al., 2016). However, no such validating study for persons with PD exists and the unique involuntary motor activity in the limbs of persons with PD, and Parkinson-related dementia and agitation, preclude extrapolation of findings from other patient populations. The

purpose of this study is therefore to test the degree of variability of sleep actigraphy scores that are generated during simultaneous placement of monitors on all four limbs (upper/lower, dominant/non-dominant limb).

2.6 Research question

The research question for this study was:

1. What are the amounts of variabilities, if they exist, in the elements of sleep that are generated by the actigraph analysis when actigraphs are placed on all four limbs of a person with PD self-reporting sleep problems (upper/lower, dominant/non-dominant limb)?

Chapter3. Methods

This chapter discusses the research methods in this study, including study design, sampling, recruitment method, inclusion and exclusion criteria, data collection, and procedures of the study and data analysis. This chapter is initially taken from the research paper Prasad and Brown, (2017) "A Pilot Study to Determine the Consistency of Simultaneous Sleep Actigraphy Measurements Comparing All Four Limbs of Patients with Parkinson Disease. *Geriatrics*, *3*(1), 1. MDPI AG. Retrieved from http://dx.doi.org/10.3390/geriatrics3010001" of which this thesis is a part.

3.1 Study design

An observational case study design was employed in the study. Observational case study is beneficial in assessing potential causation in exposure-outcome relationships (Thiese, 2014). An investigator in an observational study is not acting upon the participants but instead observing natural relationships between factors and outcomes (Thiese, 2014). Observational case studies are very cost effective and are a starting point for hypothesis generation (Leon, Davis, & Kraemer, 2011; Thiese, 2014).

3.2 Sampling

The study used convenience sampling (Marshall, 1996). Convenience sampling gives an easy and cost-effective way to obtain a sample of participants. Furthermore, convenience sampling is a useful tool for pilot studies where instruments may still be under development (Marshall,

1996). However, a disadvantage is that the result obtained is not generalizable to the population (Marshall, 1996). There have been no earlier studies of this question, and so a power calculation was not possible.

3.3 Recruitment

Recruitment of participants was through the University of Alberta Faculty of Rehabilitation student-lead teaching clinics. Clinic co-ordinators not involved in this study mailed potential participants an envelope with information materials and the consent form for the study. The addresses were put on by the representative of the student-led teaching clinics so that the researcher had no access to identifiers of potential participants until they contact him. Interested participants contacted the principal investigator (PI) by mail or telephone, whichever was preferable, and sent back a copy of the signed consent form in the stamped addressed envelope provided in the information pack. The study (Pro00071508) was approved by the Human Research Ethics Boards (REB 2) administered by the University of Alberta, and all participants gave written informed consent prior to participation in the study

3.4 Inclusion and exclusion criteria

Individuals were eligible for inclusion if they have PD and self-reported as having sleep problems. Participants underwent a screening test for cognitive impairment through the Montreal Cognitive Assessment (MoCA). Participants with a score of 26 or greater were included in the study. This cut-off point aligns with the study conducted by Macaskill and Nakas, (2011) which reported the optimal screening cut-off of less than 26 for PD- Mild Cognitive Impairment.

Participants living independently or with a family member in the Edmonton community were included in the study.

Participants were excluded from the study if on screening for cognitive assessment they score less than 26 on MoCA or if they were living in a care home.

Age, gender, and length of time since diagnosis of Parkinson disease were collected but were not exclusion criteria.

3.5 Data collection

1. Baseline assessment.

i. The Montreal Cognitive Assessment (MoCA) has been widely used in PD research and is considered to be more sensitive to executive function than the Mini-Mental Status Exam (Lessig, Nie, Xu, & Corey-Bloom, 2012; Macaskill & Nakas, 2011). The MoCA is scored out of 30 and score less than 26 indicates lower cognitive functioning. The cut-off point less than 26 is based on a study done by Macaskill and Nakas (2011), which found that scores less than 26 provided a suitable and valid basis for assessment of mild-cognitive impairment.

ii. The Hauser diary (on/off activity diary), a self- reported measure of sleep in persons with PD, was used. Hauser diaries have shown good test-retest reliability (Hauser, Deckers, & Lehert, 2004). A study done by Hauser, Deckers, & Lehert, (2004) showed the coefficient of reliability as calculated by Cronbach's α to be as follows: 2 days, r = 0.806; 3 days, r =

0.868; 4 days, r =0.918; 5 days, r = 0.934 High coefficient of alpha indicates that the diary is sufficiently reliable to be used over n (n=1,2,3,..) number of days.

iii. The Movement Disorder Society-Unified Parkinson Disease Rating Scale (MDS-UPDRS) has reported acceptable levels of validity and inter-rater reliability (Lang et al., 2013). A study done by Goetz et al.,(2008) reported that the MDS-UPDRS showed high internal consistency (Cronbach's alpha = 0.79–0.93 across parts) and correlated with the original UPDRS (ρ=0.96). The MDS-UPDRS part III was used for motor examination of the persons with Parkinson disease.

2. Primary outcomes.

i. The ActiGraph wGT3X-BT (Pensacola, FL, USA) was used to collect periods of nighttime sleep onset, maintenance, duration and other sleep quality indicators. The proprietary Actilife 6 software package (version 20.0, Pensacola, FL, USA, 2017) was set to the Cole-Kripe Sleep Scoring Algorithm option recommended for adult populations, and the data collection epochs were set at the longest possible duration (60 s) to minimize as much as a possible the recording of involuntary movements.

3.6 Procedure

Printed study invitations with information, consent form and a stamped return envelope, were sent to persons with PD who attended the University of Alberta, Faculty of Rehabilitation Medicine student-lead teaching clinics. The clinic coordinators were not involved in this study, and they addressed and mailed out the packs. Participants were asked to contact the PI by telephone or e-mail, and a meeting was scheduled at their preferred place. If the participant

consented to be in the study s/he had to complete the MoCA and was screened to determine if they fulfill the inclusion criteria by scoring more than the cut-off point (greater than 26) (Macaskill & Nakas, 2011). Eligible volunteers were provided with an MDS-UPDRS part III assessment of motor function, a demonstration of how to care for and place the ActiGraph wGT3X-BT on all four limbs (it had to be worn before going to bed and removed after waking up), and a sleep diary to record for one week. Demonstration and advice were given to the patients and family members, if present, regarding the use and placement sites of the ActiGraph wGT3X-BT and contact information for the PI to call if there were any questions. After one week, the PI visited the participant's home to collect the devices and sleep diary.

3.7 Data analysis

Data analysis was done using the Cole-Kripe Sleep Scoring Algorithm option recommended for adult populations, and the data collection epochs were set at the longest possible duration (60s) to minimize as much as a possible the recording of involuntary movements. The algorithm calculated sleep onset latency (SOL), total sleep time (TST), wake after sleep onset (WASO), number of awakenings (NA), and overall sleep efficiency (SE). Descriptive analysis was carried out to determine the range and variance of findings comparing all four limbs within each participant.

Chapter4. Results

This chapter presents the results of the study, including demographics of the participants and findings of the actigraph monitors. Descriptive data of the actigraph monitors are presented in tables in range and average format. All tables are in Appendix I. This chapter is initially taken from the research paper Prasad and Brown, (2017) "A Pilot Study to Determine the Consistency of Simultaneous Sleep Actigraphy Measurements Comparing All Four Limbs of Patients with Parkinson Disease. *Geriatrics*, *3*(1), 1. MDPI AG. Retrieved from http://dx.doi.org/10.3390/geriatrics3010001" of which this thesis is a part.

4.1 Participants involvement and demographics

Initially, 8 participants showed interest in the study. Only 4 participants out of 8 completed the study. All participants who completed the study were male, with an age range of 54-79 years and mean age of 72.5 years (Table 1). The comparative data across all four limbs are detailed in Table 2. The spread in sleep actigraphy scores for SE, TST, NA, and WASO, recorded in the dominant arm were similar to the scores in non-dominant arm (Table 3). As found in the upper limbs, the spread in sleep variable scores comparing left and right lower limbs was also similar (Table 3). However, on average, for each participant, the WASO scores were higher in the right lower limb than left lower limb (Table 3). Comparing each participant's right upper limb to his right lower limb revealed that the right upper limb score for sleep efficiency was higher (Table 3). Conversely, the right lower limb NA scores were lower than the right upper limb NA scores (Table 3). Notably, WASO scores for the right lower limb were markedly less than the WASO scores for the right upper limb. For all four participants, the SE and TST scores were less from

the lower limb monitors as compared to the upper limb monitors. Upper limb monitors generated slightly higher NA and WASO scores when compared to lower limbs. As illustrated in Table 3, TST and WASO were the least stable readings with the widest variance in scores across the four limbs.

4.2 Discussion

When placed simultaneously on all four limbs the monitors revealed that there were minimal differences in the measurement of the sleep variables (SE, TST, WASO, NA) between the dominant and non-dominant arm. These findings are similar to Maglione et al., (2013), whose analysis found that there were minimal differences in the measurement of the sleep variables between the dominant and non-dominant arm.

However, there was notable discrepancy seen in particular lower and upper limb scores. When compared to both upper limbs, SE and TST scores were higher in both lower limbs. Our findings hence suggest that there is an overestimation of sleep quality and duration when the actigraph is placed on the lower limbs. One reason for such finding can be attributed to upper extremity tremors and other motor problems such as lower limb rigidity that might interfere with actigraph readings (Slater et al., 2015). These findings align with previous findings that actigraphs placed on healthy young adults at hip level tend to overestimate sleep (Slater et al., 2015). Conversely, it is possible that actigraphy placement on upper limbs leads to underestimation of sleep. More extensive studies using PSG and/or subjective tools such as PDSS, will be required to determine the nuances of this question.

The number of awakenings (NA) and WASO scores were markedly decreased in lower limbs when compared to upper limbs. We speculated that these findings might be due to poor detection of the awake state when the monitor is placed on the ankle of someone with Parkinson-related motor impairment. As mentioned previously, these findings align with past studies of healthy adults which reported that monitor placement at hip level yields lower NA and WASO scores due to poor sleep detection (Slater et al., 2015). Coupled with the PD motor complications mentioned earlier, this suggests that actigraphy placement at the hip or ankle is not reliable for this population. Our pilot study results found that overall considerable variability exists in simultaneously collected sleep indicator scores within an individual when actigraphs are placed on different sites. These results are similar to previous studies of preschoolers and high-altitude travelers (Latshang et al., 2016). However, for persons with PD, issues of dementia and agitation, tremor, and rigidity are all considerations that can complicate the selection of the actigraph placement site. The lack of evidence-based guidelines for actigraphy use specific to the Parkinson population is an essential gap in the research and further studies, with subjective tools such as PDSS, SCOPA-S or objective tools such as PSG and video recording comparators, are required to refine our understanding of the issues that are related to selecting actigraph placement sites for persons with PD.

Although there has been increasing use of actigraphy to quantitatively record some of the symptoms of PD (such as activity and sleep disturbance), no studies so far have undertaken an evaluation to guide the placement of actigraphs in research protocols. Thus, this study contributes critical preliminary data to deepen our understanding of the use of sleep actigraphy in studies involving persons with PD. A specific recommendation that can be made at this point for studies involving intrapersonal comparisons is to maintain the same placement site across all of

the nights, and if relocation of the monitor is required because of discomfort or agitation, then the data collection should be restarted.

4.3 Limitations

Small sample size of the study implied that the results of the study could not be applied to the whole target population (i.e., persons with PD). Also, our sample excluded people with PD who had greater than mild dementia and the influence of this remains to be studied. Therefore, lack of generalizability and small sample size were essential limitations of the study. This study is the first of its kind and a power calculation to determine sample size was not possible. Another limitation of the study was the lack of PSG benchmarking or any other sleep assessment tools (such as videography or subjective sleep assessment tools) to compare our data.

One participant reported difficulties applying the actigraphs. Although no one else reported problems, the possibility of compromised data because of problems wearing the actigraphs exists. Additionally, due to lack of other objective tools such as PSG and subjective tools such as SCOPA-S, data recorded by the actigraphs could not be compared to sleep indicators that were not motion dependent. Future efforts are needed to build on this preliminary study and guide suitable placement sites for sleep actigraphy use in research involving persons with PD.

4.4 Implications

The literature demonstrates acceptance of the use of actigraphy as an objective assessment tool for sleep disorders in medical and neurobehavioral problems (Ancoli-Israel et al., 2003; Sadeh,

2011). However, there is paucity of evidence to support a guideline for application of actigraphy in persons with PD.

One reason for this lack of evidence can be attributed to the complexity of PD itself. Persons with PD suffering from sleep problems usually have motor problems (rigidity, tremor, dyskinesia and bradykinesia), and motor fluctuation may lead to a biased assessment of sleep patterns when using actigraph algorithms to convert frequency and duration of movement in multiple planes into sleep variables. Furthermore, there are various commercially available actigraphs which use different algorithms and methodologies and have dissimilarity in regard to the detection and recording of movements (Ancoli-Israel et al., 2003; Sadeh, 2011; Tryon, 2004). Also, the literature does not mention appropriate guidelines for an optimal scoring parameter concerning actigraphy in persons with PD. Furthermore, there are inconsistencies between the studies concerning the optimal placement site. Guidelines for actigraphy recommend placing the monitor on the non-dominant wrist (Ray et al., 2014). However, this potentially can be the most involved limb for someone with Parkinson disease (Sveinbjornsdottir, 2016). Similar to a study done by Maglione et al.,(2013), we found minimal differences in measured sleep variables between dominant and non-dominant arm when actigraphs are placed simultaneously on both arms. Procuring minimal differences in sleep variables from both dominant and non-dominant arm raises uncertainty about the conventional recommendation of placing the actigraph on the non-dominant wrist.

We also found that sleep indicators such as SE and TST were higher in lower limbs. This aligns with previous studies on other populations which have suggested that lower limbs tend to overestimate sleep. However as discussed earlier, symptoms such as tremors and rigidity, can influence actigraphs which are placed on upper limbs. This may explain why we found SE and

TST scores higher in lower limbs. Hence, there is a need to look into the predicament of measurement of sleep variables in upper limbs and lower limbs.

These findings suggest that we need to congregate evidence concerning optimal placement site for actigraphs on persons with PD. Furthermore, it is of utmost importance to set up guidelines and procedural protocols concerning optimal sleep parameters and optimal placement sites, when using actigraphy in persons with PD.

Chapter5. Conclusion

Over the last two decades, actigraphy has become an accessible and widely used assessment tool in sleep research and clinical practice. However, knowledge concerning the implementation of actigraphy in studies of persons with PD is sparse. One of the most critical parts is the placement of the actigraph. Literature has mentioned the ideal placement site to be the non-dominant wrist (Ray et al., 2014). However, in persons with PD, the non-dominant wrist possibly might be the most affected limb. The small sample size and lack of comparison tools, such as PSG and self-report tools such as SCOPA-S, did not allow us to find conclusive evidence about the placement of the actigraph. This study contributes preliminary data concerning suitable actigraph placement site depending on the sleep indicators of interest. This research also suggests that placement of the actigraph on either the dominant or non-dominant wrist may not affect specific sleep scores to the extent that placement on upper versus lower limbs would have. Furthermore, the possibility of over and underestimation of sleep scores dependent on limb placement will require closer study with simultaneous PSG and/or subjective self-report tools. We are only able to speculate at this time, and further research is much needed in this regard.

Reflection

Sleep problems are common in persons with PD, and approximately 50% to 70 % of persons with PD have some form of sleep disorder (Selvaraj & Keshavamurthy, 2016). We can contemplate that these 50 % to 70% persons with PD should undergo sleep assessment at some point during the disease. There are clinical scales for the evaluation of sleep disorders in persons with PD; these scales are observational and self-report and therefore do not necessarily adequately and quantitatively reflect the sleep problem severity nor capture sufficient before and after outcome data for research. There are also objective tools which can adequately and quantitatively reflect the sleep problems. However, these objective tools can only be employed in hospital settings and are costly.

Presence of motor symptoms such as rigidity, postural tremors, dyskinesia, and bradykinesia affect the mobility of persons with PD, and it can be a tedious task for a person with PD to visit the hospital for a sleep assessment. Also, having a sleep assessment adds burden of cost to the patient and their caregivers.

Literature, however, mentions the use of objective tools such as the actigraph which is cost-effective, reliable, and sensitive to sleep variables (such as sleep onset, maintenance, duration, and nighttime awakenings). In the last decade or so, wrist actigraphy which is a form of objective sleep parameter has gained a central role as an objective assessment tool in sleep research and clinical settings (Sadeh, 2011).

When we compare actigraph to overnight polysomnography (PSG) for assessment of sleep, actigraphy offers several advantages that make it more appealing to researchers and clinicians. For example, actigraphy is cost-effective, does not require sleeping in a lab, and studies have

reported actigraph to be more feasible for use over extended periods of time (i.e., days to weeks), hence allowing the collection of data about day to day variability in sleep patterns (Sadeh, 2011). Further, actigraph provides information about sleep and wake patterns in a patient's natural sleep environment (Maglione et al., 2013; Stavitsky et al., 2010).

While examining evidence supporting the application of actigraph in persons with PD, I found inconsistency among the studies concerning sleep parameters, algorithm used, and placement sites. I comprehended that to practice actigraphy optimally in persons with PD; we need to have a guideline and procedure protocol concerning optimal sleep parameters and placement site. Studies in different population samples suggest non-dominant wrist as the optimal site for placing monitor. However, this potentially can be the most affected limb for a person with PD (Sveinbjornsdottir, 2016).

Hence, I thought to do a small study to examine the probable best placement site in persons with PD. This study provided me a lot of learning experience and helped me to grow as a researcher. While writing the proposal, I had no idea about the sample size needed for the study. Being the very first study to look into the placement sites, I thought to start with a small sample size as it would provide baseline evidence to build a strong case afterward.

After completion of the study, I have presented my results at various conference and seminars. At these meetings when I talk about my work, I get a decent response from my peer researchers, and they provide invaluable suggestions which have enhanced my knowledge about the applications and gap of knowledge in the research field concerning actigraphy.

The results from the study has provided evidence which suggests that maybe placement on either dominant or non-dominant wrist does not affect sleep parameter and maybe upper limbs are

better placement sites for placing actigraphs in persons with PD. However, further investigation on a larger scale is needed to establish these facts.

References

Ancoli-Israel, S., Cole, R., Alessi, C., Chambers, M., Moorcroft, W., & Pollak, C. P. (2003). The role of actigraphy in the study of sleep and circadian rhythms. *Sleep*, *26*(3), 342–392.

Ataide, M., Franco, C. M. R., & Lins, O. G. (2014). Daytime sleepiness and Parkinson's disease: the contribution of the multiple sleep latency test. *Sleep Disorders*, *2014*, 767181. https://doi.org/10.1155/2014/767181

Banks, S., & Dinges, D. F. (2007). Behavioral and physiological consequences of sleep restriction. *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *3*(5), 519–28. https://doi.org/10.1055/s-0029-1237117.Neurocognitive

Calogiuri, G., Weydahl, A., & Carandente, F. (2011). Methodological Issues for Studying the Rest-Activity Cycle and Sleep Disturbances: A Chronobiological Approach Using Actigraphy Data. *Biological Research For Nursing*, *15*(1), 5–9. https://doi.org/10.1177/1099800411416224

Chen, J. H., Waite, L., Kurina, L. M., Thisted, R. A., McClintock, M., & Lauderdale, D. S. (2015). Insomnia symptoms and actigraph-estimated sleep characteristics in a nationally representative sample of older adults. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, *70*(2), 185–192. https://doi.org/10.1093/gerona/glu144

Chin-Chan, M., Navarro-Yepes, J., & Quintanilla-Vega, B. (2015). Environmental pollutants as risk factors for neurodegenerative disorders: Alzheimer and Parkinson diseases. *Frontiers in Cellular Neuroscience*, *9*, 124. https://doi.org/10.3389/fncel.2015.00124

dos Santos, A. B., Kohlmeier, K. A., & Barreto, G. E. (2015). Are Sleep Disturbances Preclinical Markers of Parkinson's Disease? *Neurochemical Research*, *40*(3), 421–427. https://doi.org/10.1007/s11064-014-1488-7

Elbaz, A. (2016). Prodromal symptoms of Parkinson's disease: Implications for epidemiological studies of disease etiology. *Revue Neurologique*, *172*(8–9), 2–10. https://doi.org/10.1016/j.neurol.2016.07.001

Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., … Zweig, R. M. (2008). Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders*, *23*(15), 2129–2170. https://doi.org/10.1002/mds.22340

Hauser, R. A., Deckers, F., & Lehert, P. (2004). Parkinson's disease home diary: Further validation amd implications for clinical trials. *Movement Disorders*, *19*(12), 1409–1413. https://doi.org/10.1002/mds.20248

Hislop, J., Palmer, N., Anand, P., & Aldin, T. (2016). Validity of wrist worn accelerometers and comparability between hip and wrist placement sites in estimating physical activity behaviour in preschool children. *Physiological Measurement*, *37*(10), 1701–1714. https://doi.org/10.1088/0967-3334/37/10/1701

Högl, B., Arnulf, I., Comella, C., Ferreira, J., Iranzo, A., Tilley, B., … Goetz, C. G. (2010). Scales to assess sleep impairment in Parkinson's disease: Critique and recommendations. *Movement Disorders*, *25*(16), 2704–2716. https://doi.org/10.1002/mds.23190

Jahan, I., Hauser, R. A., Sullivan, K. L., Miller, A., & Zesiewicz, T. A. (2009). Sleep disorders in Parkinson's disease. *Neuropsychiatric Disease and Treatment*, *5*(1), 535–540.

https://doi.org/10.1097/NRL.0b013e31823966f8

Knie, B., Mitra, M. T., Logishetty, K., & Chaudhuri, K. R. (2011). Excessive Daytime Sleepiness in Patients with Parkinson' s Disease. *CNS Drugs*, *25*(3), 203–212.

Kotschet, K., Johnson, W., McGregor, S., Kettlewell, J., Kyoong, A., O'Driscoll, D. M., … Horne, M. K. (2014). Daytime sleep in Parkinson's disease measured by episodes of immobility. *Parkinsonism and Related Disorders*, *20*(6), 578–583. https://doi.org/10.1016/j.parkreldis.2014.02.011

Kumar, S., Bhatia, M., & Behari, M. (2002). Sleep Disorders in Parkinson ' s Disease. *Society*, *17*(4), 775–781. https://doi.org/10.1002/mds.10167

Kummer, A., & Teixeira, A. L. (2009). Neuropsychiatry of Parkinson's disease. *Arquivos de Neuro-Psiquiatria*, *67*(3 B), 930–939. https://doi.org/10.1590/S0004-282X2009000500033

Kushida, C. A., Littner, M. R., Morgenthaler, T., Alessi, C. A., Bailey, D., Coleman, J., … Wise, M. (2005). Practice Parameters for the Indications for Polysomnography and Related Procedures: An Update for 2005. *Sleep*, *28*(4), 499–523. https://doi.org/10.1093/sleep/28.4.499

Lang, A. E., Eberly, S., Goetz, C. G., Stebbins, G., Oakes, D., Marek, K., … Shoulson, I. (2013). Movement disorder society unified parkinson disease rating scale experiences in daily living: Longitudinal changes and correlation with other assessments. *Movement Disorders*, *28*(14), 1980–1986. https://doi.org/10.1002/mds.25671

Latshang, T. D., Mueller, D. J., Lo Cascio, C. M., Stöwhas, A.-C., Stadelmann, K., Tesler, N., … Bloch, K. E. (2016). Actigraphy of Wrist and Ankle for Measuring Sleep Duration in

Altitude Travelers. *High Altitude Medicine & Biology*, *0*(0), ham.2016.0006. https://doi.org/10.1089/ham.2016.0006

Leon, A. C., Davis, L. L., & Kraemer, H. C. (2011). The role and interpretation of pilot studies in clinical research. *Journal of Psychiatric Research*, *45*(5), 626–629. https://doi.org/10.1016/j.jpsychires.2010.10.008

Lessig, S., Nie, D., Xu, R., & Corey-Bloom, J. (2012). Changes on brief cognitive instruments over time in Parkinson's disease. *Movement Disorders*, *27*(9), 1125–1128. https://doi.org/10.1002/mds.25070

Lowe, C. J., Safati, A., & Hall, P. A. (2017). The neurocognitive consequences of sleep restriction: A meta-analytic review. *Neuroscience and Biobehavioral Reviews*, *80*(July), 586–604. https://doi.org/10.1016/j.neubiorev.2017.07.010

Lugaresi, E., & Provini, F. (2001). Sleep and movement disorders. *Sleep and Hypnosis*, *3*(2), 55–61. https://doi.org/10.1007/s10072-005-0482-x

Macaskill, M. R., & Nakas, C. T. (2011). The MoCA : Well-suited screen for cognitive impairment in Parkinson disease The MoCA Well-suited screen for cognitive impairment in Parkinson disease, 1717–1725. https://doi.org/10.1212/WNL.0b013e3181fc29c9

Maglione, J. E., Liu, L., Neikrug, A. B., Poon, T., Natarajan, L., Calderon, J., … Ancoli-Israel, S. (2013). Actigraphy for the assessment of sleep measures in Parkinson's disease. *Sleep*, *36*(8), 1209–17. https://doi.org/10.5665/sleep.2888

Mahlknecht, P., Seppi, K., & Poewe, W. (2015). The concept of prodromal Parkinson's disease. *Journal of Parkinson's Disease*, *5*(4), 681–697. https://doi.org/10.3233/JPD-150685

Mantua, J., Gravel, N., & Spencer, R. M. C. (2016). Reliability of sleep measures from four personal health monitoring devices compared to research-based actigraphy and polysomnography. *Sensors (Switzerland)*, *16*(5). https://doi.org/10.3390/s16050646

Margis, R., Donis, K., Sch??nwald, S. V., Fagondes, S. C., Monte, T., Mart??n-Mart??nez, P., … Rieder, C. R. M. (2009). Psychometric properties of the Parkinson's Disease Sleep Scale - Brazilian version. *Parkinsonism and Related Disorders*, *15*(7), 495–499. https://doi.org/10.1016/j.parkreldis.2008.12.008

Marinus, J., Visser, M., van Hilten, J. J., Lammers, G. J., & Stiggelbout, A. M. (2003). Assessment of sleep and sleepiness in Parkinson disease. *Sleep*, *26*(8), 1049–54. Retrieved from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14746389%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/14746389

Marshall, M. N. (1996). Sampling for qualitative research Sample size. *Family Practice*, *13*(6), 522–525. https://doi.org/10.1093/fampra/13.6.522

Martinez-Martin, P., Visser, M., Rodriguez-Blazquez, C., Marinus, J., Chaudhuri, K. R., van Hilten, J. J., … Arroyo, S. (2008). SCOPA-sleep and PDSS: Two scales for assessment of sleep disorder in Parkinson's disease. *Movement Disorders*, *23*(12), 1681–1688. https://doi.org/10.1002/mds.22110

Melegari, M. G., Vittori, E., Mallia, L., Devoto, A., Lucidi, F., Ferri, R., & Bruni, O. (2016). Actigraphic Sleep Pattern of Preschoolers With ADHD. *Journal of Attention Disorders*. https://doi.org/10.1177/1087054716672336

Muntean, M.-L., Benes, H., Sixel-Döring, F., Chaudhuri, K. R., Suzuki, K., Hirata, K., …

Trenkwalder, C. (2016). Clinically relevant cut-off values for the parkinson's disease sleep scale-2 (PDSS-2): a validation study. *Sleep Medicine*, *24*, 87–92. https://doi.org/10.1016/j.sleep.2016.06.026

Pan, W., Kwak, S., Li, F., Wu, C., Chen, Y., Yamamoto, Y., & Cai, D. (2013). Actigraphy monitoring of symptoms in patients with Parkinson's disease. *Physiology & Behavior*, *119*, 156–60. https://doi.org/10.1016/j.physbeh.2013.05.044

Peralta, C. M., Frauscher, B., Seppi, K., Wolf, E., Wenning, G. K., Högl, B., & Poewe, W. (2009). Restless legs syndrome in Parkinson's disease. *Movement Disorders*, *24*(14), 2076–2080. https://doi.org/10.1002/mds.22694

Prasad, V., & Brown, C. (2017). A Pilot Study to Determine the Consistency of Simultaneous Sleep Actigraphy Measurements Comparing All Four Limbs of Patients with Parkinson Disease. *Geriatrics*, *3*(1), 1. https://doi.org/10.3390/geriatrics3010001

Ray, M. A., Youngstedt, S. D., Zhang, H., Robb, S. W., Harmon, B. E., Jean-Louis, G., … Burch, J. B. (2014). Examination of wrist and hip actigraphy using a novel sleep estimation procedure. *Sleep Science*, *7*(2), 74–81. https://doi.org/10.1016/j.slsci.2014.09.007

Sadeh, A. (2011). The role and validity of actigraphy in sleep medicine: An update. *Sleep Medicine Reviews*, *15*(4), 259–267. https://doi.org/10.1016/j.smrv.2010.10.001

Samson, D. R., Yetish, G. M., Crittenden, A. N., Mabulla, I. A., Mabulla, A. Z. P., & Nunn, C. L. (2016). What is segmented sleep? Actigraphy field validation for daytime sleep and nighttime wake. *Sleep Health*, *2*(4), 341–347. https://doi.org/10.1016/j.sleh.2016.09.006

Selvaraj, V. K., & Keshavamurthy, B. (2016). Sleep dysfunction in Parkinson's disease. *Journal*

of Clinical and Diagnostic Research, *10*(2), OC09-OC12. https://doi.org/10.3748/wjg.v22.i25.5742

Shpirer, I., Goldstein, R., Miniovitz, A., Klein, C., Prokhorov, T., Theitler, J., … Rabey, J. M. (2007). Reply: Excessive daytime sleepiness in patients with Parkinson's disease: A polysomnography study [7]. *Movement Disorders*, *22*(10), 1520–1521. https://doi.org/10.1002/mds.21487

Slater, J. A., Botsis, T., Walsh, J., King, S., Straker, L. M., & Eastwood, P. R. (2015). Assessing sleep using hip and wrist actigraphy. *Sleep and Biological Rhythms*, *13*(2), 172–180. https://doi.org/10.1111/sbr.12103

Stavitsky, K., Saurman, J. L., McNamara, P., & Cronin-Golomb, A. (2010). Sleep in Parkinson's disease: A comparison of actigraphy and subjective measures. *Parkinsonism and Related Disorders*, *16*(4), 280–283. https://doi.org/10.1016/j.parkreldis.2010.02.001

Sveinbjornsdottir, S. (2016). The clinical symptoms of Parkinson's disease. *Journal of Neurochemistry*, *139*, 1–7. https://doi.org/10.1111/jnc.13691

Takács, J., Bódizs, R., Ujma, P. P., Horváth, K., Rajna, P., & Harmat, L. (2016). Reliability and validity of the Hungarian version of the Pittsburgh Sleep Quality Index (PSQI-HUN): comparing psychiatric patients with control subjects. *Sleep and Breathing*, 1045–1051. https://doi.org/10.1007/s11325-016-1347-7

The Government of Canada. (2014). *Mapping Connections an Understanding of Neurological Conditions*. https://doi.org/978-1-100-24442-6

Thiese, M. S. (2014). Special Lessons issue : in biostatistics Responsible writing in science

Observational and interventional study design types ; an overview, *24*(2), 199–210.

Tolleson, C. M., Bagai, K., Walters, A. S., & Davis, T. L. (2016). A Pilot Study Assessing the Effects of Pallidal Deep Brain Stimulation on Sleep Quality and Polysomnography in Parkinson's Patients. *Neuromodulation*, *2016*, 724–730. https://doi.org/10.1111/ner.12442

Tryon, W. W. (2004). Issues of validity in actigraphic sleep assessment. *Sleep*, *27*(1), 158–165.

Visanji, N., & Marras, C. (2015). The relevance of pre-motor symptoms in Parkinson's disease. *Expert Review of Neurotherapeutics*, *15*(10), 1205–1217. https://doi.org/10.1586/14737175.2015.1083423

Wallén, M. B., Nero, H., Franzén, E., & Hagströmer, M. (2014). Comparison of two accelerometer filter settings in individuals with Parkinson's disease. *Physiological Measurement*, *35*, 2287–2296. https://doi.org/10.1088/0967-3334/35/11/2287

Zea-Sevilla, M. A., & Martínez-Martín, P. (2014). Rating scales and questionnaires for assessment of sleep disorders in Parkinson's disease: What they inform about? *Journal of Neural Transmission*, *121*(SUPPL. 1). https://doi.org/10.1007/s00702-014-1217-z

Zinkhan, M., Berger, K., Hense, S., Nagel, M., Obst, A., Koch, B., … Stang, A. (2014). Agreement of different methods for assessing sleep characteristics: A comparison of two actigraphs, wrist and hip placement, and self-report with polysomnography. *Sleep Medicine*, *15*(9), 1107–1114. https://doi.org/10.1016/j.sleep.2014.04.015

Appendix I

Table 1. Demographics

	Gender	Age (Years)	Right Hand Dominance	MoCA	UPDRS Part III Aggregate Score	H &Y Stage
Participant 1	**M**	**54**	**Yes**	**29**	**35**	**2**
Participant 2	**M**	**83**	**Yes**	**27**	**72**	**3**
Participant 3	**M**	**71**	**Yes**	**28**	**52**	**2**
Participant 4	**M**	**79**	**Yes**	**27**	**58**	**2**
Mean		**72.5**		**27.75**	**54.25**	**2**

Key: MoCA = Montreal cognitive assessment; MDS-UPDRS = Movement Disorders Society Sponsored Unified Parkinson's Disease Rating Scale; H & Y Stage = Hoehn-Yahr Stage.

Table 2. Actigraph readings across participants with simultaneous limb placement (rounded off to nearest whole number).

	Participant 1	Participant 2	Participant 3	Participant 4
Right lower limb				
SE (%)	**65–83**	**98–100**	**88–96**	**87–95**
TST (min)	**283–344**	**427–448**	**369–503**	**369–495**
WASO (min)	**62–152**	**2–6**	**13–50**	**20–56**
NA	**10–15**	**1–2**	**3–11**	**4–13**
Avg. A (min)	**6–10**	**2–6**	**4–12**	**2–5**
Right upper limb				
SE (%)	**47–74**	**97–100**	**58–87**	**79–94**
TST (min)	**206–297**	**425–441**	**247–444**	**336–469**
WASO (min)	**95–229**	**1–7**	**52–181**	**35–89**
NA	**9–14**	**1–3**	**12–28**	**4–17**
Avg. A (min)	**9–16**	**1–4**	**3–6**	**3–6**
Left lower limb				
SE (%)	**76–84**	**98–100**	**82–94**	**91–96**
TST (min)	**278–364**	**427–448**	**345–490**	**387–494**
WASO (min)	**71–108**	**1–6**	**24–72**	**19–38**
NA	**9–11**	**1–2**	**5–24**	**5–12**
Avg. A (min)	**7–14**	**1–6**	**3–5**	**3–5**
Left upper limb				
SE (%)	**46–67**	**98–100**	**59–83**	**87–94**

TST (min)	**202–298**	**427–448**	**246–443**	**380–461**
WASO (min)	**134–233**	**1–7**	**70–167**	**20–57**
NA	**8–13**	**1–4**	**12–34**	**3–15**
Avg. A (min)	**10–18**	**1–4**	**4–7**	**3–9**

Key: SE = sleep efficiency; TST = total sleep time; WASO = wake after sleep onset; NA = number of awakening; Avg. A = average awakening

Table 3. The within-participant variance of actigraph scores.

	Participant 1 Range	Participant 2 Range	Participant 3 Range	Participant 4 Range
Lower limbs				
SE (%)	**65.06–83.78**	**98.62–99.54**	**82.14–96.14**	**86.82–95.71**
TST (min)	**278–364**	**427–448**	**345–503**	**369–495**
WASO (min)	**62–152**	**1–6**	**13–72**	**19–56**
NA	**9–15**	**1–4**	**3–24**	**4–13**
Avg. A(min)	**6–14**	**1–6**	**3–12**	**3–5**
Upper limbs				
SE (%)	**46.44–73.61**	**96.92–99.77**	**57.58–87.38**	**79.06–94.13**
TST (min)	**202–298**	**416–448**	**246–444**	**336–469**
WASO (min)	**95–233**	**1–7**	**52–181**	**20–89**
NA	**8–14**	**1–4**	**12–34**	**3–17**
Avg. A (min)	**9–18**	**1–4**	**3–7**	**3–9**

Key: SE = sleep efficiency; TST = total sleep time; WASO = wake after sleep onset; NA = number of awakenings; Avg. A = average awakening.

Appendix II Information and consent form

INFORMATION LETTER and CONSENT FORM

Study Title: A pilot study to determine the consistency of sleep actigraphy measurements comparing all four limbs of patients with Parkinson's disease.

Research Investigator:

Vineet Prasad

MSc rehabilitation science student

Faculty of Rehabilitation Medicine

1-45 Corbett Hall

University of Alberta

Edmonton, AB, T6G2G4

vp@ualberta.ca

780-492-1728

Supervisor:

Cary A Brown

FHEA, PhD

Acting Chair and Professor

Department of Occupational Therapy

Faculty of Rehabilitation Medicine

2-64 Corbett Hall

University of Alberta

Edmonton, AB, T6G2G4

cary1@ualberta.ca

Dear Sir/Madam,

You are receiving this letter and information pack because you were/are a patient in Corbett Clinic. The clinic co-ordinator mailed the envelope to you, and we have not seen your name.

We would like to invite you to take part in a study to assist us to understand if the limb you wear a sleep monitor on will make a difference to the readings. As you know, many people with Parkinson disease have trouble sleeping. One tool used in research to measure sleep is called an actigraph. It looks like a wrist watch, and you wear it on your arm or sometimes on the ankle. For people with Parkinson disease, there has not been a study to clearly tell us if it matters what arm or leg the monitor is worn on and how much variation there might be in actigraph findings between all four limbs. We are hoping you would be interested in volunteering for a study to examine this.

Purpose

The goal of this study is to explore if wearing the sleep actigraph on different limbs will result in the actigraph taking the same, or different readings. For example, will an actigraph worn on the left ankle take the same readings as one worn on the right wrist? The results of the study will assist us to have a more accurate way to determine the outcome of sleep interventions in other studies.

What are we asking you to do?

Please contact the PI by phone telephone (780-492-1728) or e-mail (vp@ualberta.ca) to get more information and to set up a meeting in a location that is convenient for you. Please sign the consent form provided in this information pack and return it to the researchers in the enclosed stamped envelope.

Once we have your consent form we can start the study- first, we will ask you some questions to determine if you are a match for the study participant criteria. That will involve a baseline test of your motor function and some memory and concentration questions.

After that, we ask that you wear an actigraph on each limb for 1 week (it has to be worn before going to bed and removed after waking up). Actigraphs are small like a wrist watch, and they have an adjustable strap so you can wear it under or on top of your clothing, whatever is most comfortable for you. Also, you will need to keep a sleep diary to record when you go to bed and when you get up. We will give you, and anyone else in the family who is interested, a full demonstration. You can ask questions at any time. You will also have our contact information to call if there are any questions. After one week, we will visit your home to collect the sleep actigraphs and sleep diary.

Benefits

You will not benefit directly from being in this study. Your participation will help us in understanding the best limb placement for actigraphs in studies to measure sleep treatments for people with Parkinson disease.

There is no cost involved in being in the research.

We can't offer you any financial compensation by participating in the study but you will receive a full sleep report from the actigraphs, and we will explain what it means to you.

Risk

We are not aware of any risks to being in this study. If we learn anything from the research that may affect your willingness to continue being in the study, we will tell you right away. None of the therapists at Corbett Clinic will know if you are participating. Whether or not you participate will have no effect on your treatment from them.

Voluntary Participation

You are not obliged to participate in this study or to answer any specific questions while participating in the study.

You can drop out of the study without any penalty. You can ask to have any collected data withdrawn from the database and not included in the study up until 1 week after the study finishes. After that, the data will have been combined with others and analyzed so we cannot remove it.

Confidentiality & Anonymity

The research result will be used for research articles. You will not be personally identified in the research reports.

Directly identifying information, such as your name, shall be removed from the information and you shall be assigned a code number for identification purpose. The data collection forms and records will only reflect the code number. The master list linking codes to personal details will be stored in a separate locked drawer in the lab and will be destroyed as soon as all data has been inputted to maximize the security of your information. Electronic data will be secured in Dr. Brown's password protected lab computer.

Data will be kept confidential, and only the principal investigator (Vineet Prasad) and his supervisor (Dr. Cary Brown), will have access to the data collected.

Further Information

If you have any further questions regarding this study, please do not hesitate to contact Vineet Prasad- vp@ualberta.ca (780-492-1728) or Cary Brown -cary.brown@ualberta.ca (780-492-9545).

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615. If you have questions about the researchers, please contact John E. Misiaszek, Associate Dean (Research), Faculty of Rehabilitation Medicine, 3-48E Corbett Hall (ph) 780.492.2412

Thank you for considering my request.

Vineet Prasad

Consent Statement

I have read this form, and the research study has been explained to me. I have been given the opportunity to ask questions, and my questions have been answered. If I have additional questions, I have been told whom to contact. I agree to participate in the research study described above and will receive a copy of this consent form. I will receive a copy of this consent form after I sign it.

_____ _____

Participant's Name (printed) and Signature Date

_____ _____

Name (printed) and Signature of Person Obtaining Consent Date

Contact information:

Phone: _____

Email: _____

Appendix III. Prasad, V., & Brown, C. (2017). A Pilot Study to Determine the Consistency of Simultaneous Sleep Actigraphy Measurements Comparing All Four Limbs of Patients with Parkinson Disease. *Geriatrics*, *3*(1), 1. MDPI AG. Retrieved from http://dx.doi.org/10.3390/geriatrics3010001