

**AN EXAMINATION OF THE RELATIONSHIPS BETWEEN NEUROPATHIC
PAIN, EXERCISE AND AFFECT IN ADULTS WITH SPINAL CORD INJURY**

by

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AN EXAMINATION OF THE RELATIONSHIPS BETWEEN NEUROPATHIC PAIN,
EXERCISE AND AFFECT IN ADULTS WITH SPINAL CORD INJURY

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Abstract

Purpose: Neuropathic pain affects up to 75% of individuals with a spinal cord injury (SCI), with many reporting pain as more disabling than the injury itself. Currently, treatments are primarily pharmaceutical, however exercise may alleviate neuropathic pain. Daily fluctuations in neuropathic pain are not well understood, specifically in relation to exercise participation. Additionally, the connection between exercise and affective mood states of adults with SCI is unclear. The purpose of this study was to utilize ecological momentary assessment to measure intra-individual diurnal variations in neuropathic pain sensations and affect. This study aimed to provide a deeper understanding of how neuropathic pain and affect change from pre- to post-exercise, and over time.

Methods: Six physically active adults with SCI participated in a 6-day study protocol. They responded to six daily prompts between 9:00 AM and 9:00 PM, and before and after exercising, using the Smartphone application mEMA. The prompts required participants to answer the Feeling Scale, Felt Arousal Scale, and a modified version of the Neuropathic Pain Scale. Neuropathic pain scores were averaged into a composite score and data were analyzed by plotting neuropathic pain and affective scores over the 6 days. Paired samples t-tests were conducted to observe changes in neuropathic pain and affect from pre- to post-exercise. Bivariate Pearson's correlational analyses were performed to observe if correlations existed between time of day, neuropathic pain and affect within-subjects.

Results: Overall, participants experienced a significant decrease in neuropathic pain ($t(5) = 3.93$; $p=0.011$) following completion of at least one bout of exercise. However, two participants experienced an increase in neuropathic pain following one bout of exercise. With regards to affect, a large, but non-significant increase ($Hg_{av}=0.76$) in Feeling Scale scores occurred following one bout of exercise. Changes in arousal were non-significant following exercise. Time of day, neuropathic pain and affect were significantly correlated for one participant.

Conclusion: These results suggest that exercise can reduce neuropathic pain, and may also increase feelings of pleasure. Further research is needed to look at both individual characteristics, and characteristics of exercise that may moderate exercise-induced changes in neuropathic pain and affect for adults with SCI.

Lay Summary

This thesis project aimed to determine whether exercise participation may reduce neuropathic pain sensations experienced by adults with spinal cord injury (SCI). Simultaneously, this study sought to observe whether pain and one's mood states are related, and whether they change over the course of a day. Despite the debilitating consequences of neuropathic pain, currently, treatments are primarily pharmaceutical in nature. Due to the side effects associated with many of these treatments, this study provides information regarding the utility of an alternative treatment to aid in reducing neuropathic pain—exercise. Furthermore, exercise may acutely increase feelings of pleasure for adults with SCI. Mapping temporal variations in neuropathic pain and mood states is of benefit for this population, to identify times of day when people may be most susceptible. Based on results from this study, exercise may be a viable option for adults with SCI who are seeking treatment for neuropathic pain.

Preface

This thesis is based on work conducted at University of British Columbia (Okanagan) by Kendra Todd, and Dr. Kathleen Martin Ginis. Kendra Todd was responsible for authoring the ethics application that was submitted to the Behavioural Research Ethics Board at University of British Columbia (Okanagan), as well as the design of the research study. Furthermore, she selected which measures would be used, and was the sole investigator responsible for participant recruitment, participant contact, training participants how to utilize the apparatus, and the conduct of exit interviews. Last, Kendra was responsible for all data collection, input and analysis. Dr. Kathleen Martin Ginis provided assistance with design of the research study, measurement selection, obtaining ethics approval, analysis and interpretation of the data. In addition, Dr. Kathleen Martin Ginis provided funding for this research study.

This research study has not yet been published.

This research study was approved by the Behavioural Research Ethics Board at the University of British Columbia (Okanagan).

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1 Introduction

Spinal cord injury (SCI) has an estimated global incidence of 40-80 cases per million population (WHO Fact Sheet, 2013) and is defined as any traumatic or non-traumatic event that damages the spinal cord and results in paralysis (Maynard et al., 1997). The level of SCI determines whether the injury results in tetraplegia or paraplegia. Tetraplegia refers to impairment or loss of motor and/or sensory functions in the cervical segments of the spinal cord and results in reduced or eliminated function and/or sensation in the arms, trunk, legs and pelvic organs (Nas et al., 2015). Paraplegia refers to impairment or loss of motor and/or sensory function in the thoracic, lumbar or sacral segments of the spinal cord. Arm functioning is spared; however, trunk, legs and pelvic organs may be impacted depending on neurological level of injury (NLI). These injuries may be complete or incomplete. Complete SCI means full loss of motor and sensory functions below the level of injury, whereas incomplete SCI refers impaired sensory and/or motor control between the NLI and the lower sacral segments (Nas et al., 2015).

Persons with SCI, regardless of NLI, are at an increased risk of secondary health complications such as pain, pressure sores, gastrointestinal and urinary disturbances, pressure ulcers, autonomic dysreflexia and cardiovascular diseases (Hagen, 2015). Although muscle paralysis is consistently referred to as the most debilitating consequence of SCI, it has been shown that neuropathic pain is often more disabling than the injury itself (Anson & Shepherd, 1995). As a result, this further impacts the ability for these individuals to return to work or socialize with friends and family.

1.1 Pain and Spinal Cord Injury

Chronic pain has been shown to affect 26-96% of the SCI population (Dijkers et al., 2009), with the average prevalence rate across studies nearing approximately 65% (Finnerup, 2013; Siddall & Loeser, 2001). Furthermore, the majority of people with SCI who suffer from chronic pain refer to their pain as severe and/or debilitating (Siddall et al., 1999). Together, these data illustrate the necessity for research to better understand and alleviate pain in the SCI population.

Inconsistent classifications of pain in the SCI population increase the difficulties of determining potential causes and treatments. In 2012, the International Spinal Cord Injury Pain (ISCIP) Classification was developed by 15 clinicians and researchers with extensive experience treating and studying SCI-related pain (Bryce et al., 2012). According to the ISCIP Classification, pain can be categorized into “tiers” including nociceptive pain, neuropathic pain, other and unknown pain. These tiers can be further subdivided. Given that pain after SCI often persists, worsens over time, and treatments have limited efficacy (Siddall et al., 2003), treatments specifically targeting each tier of pain are necessary. This thesis focuses specifically on neuropathic pain.

Neuropathic pain is defined as “pain caused by a lesion or disease of the somatosensory nervous system (IASP, 2012), and results in a multitude of sensations. Neuropathic pain has been described as burning, tingling, pricking, sharp, shooting, squeezing, cold, electric, surface and deep sensations (Hagen & Rekan, 2015). Furthermore, allodynia (pain resulting from a non-noxious stimulus) and hyperalgesia (heightened response from a noxious stimulus) are common symptoms experienced by persons with neuropathic pain (Jensen & Finnerup, 2014). Although individuals with SCI

often experience various types of pain simultaneously, neuropathic pain alone affects 29-75% of the population (Siddall et al., 2003), and is frequently considered one of the most debilitating forms of pain (Anson & Shepherd, 1995; Miroslav-Backonja & Stacey, 2004).

Neuropathic pain can be sub-categorized as at-level SCI pain, below-level SCI pain, and other neuropathic pain. At-level neuropathic pain occurs in a segmental pattern anywhere within the dermatome of the NLI and within 3 dermatomes below this level (Bryce et al., 2012). This pain is a result of a lesion or disease of a nerve root of the spinal cord. Below-level neuropathic pain refers to pain more than 3 dermatomes below the NLI (Lee et al., 2013), and is primarily caused by changes to the central nervous system as a result of the injury (Siddall et al., 1999). In contrast, neuropathic pain that does not result from a lesion, disease of a nerve root, or the spinal cord can be considered other neuropathic pain, which is suggestive of being unrelated to SCI (Bryce et al., 2012). For the purpose of this study, at-level and below-level neuropathic pain will be of primary focus.

1.2 Treatments for SCI-Related Neuropathic Pain

Neuropathic pain responds poorly to currently utilized treatments, with pharmacological treatments being the most commonly prescribed. For example, anticonvulsants, tricyclic antidepressants, opioids, and nonopioid analgesics have been considered the best forms of treatment, regardless of the negative side effects that often ensue (Guy et al., 2016; Warms et al., 2002). Anticonvulsants, such as gabapentin, pregabalin and amitriptyline have been associated with significant reductions in neuropathic pain and are considered first-line treatments for SCI-related neuropathic pain (Finnerup & Baastrop, 2012; Guy et al., 2016). The side effects of anticonvulsants include dizziness, edema, dry mouth, fatigue, and

drowsiness (Cardenas et al., 2013; Kukkar et al., 2013). Antidepressants are also often prescribed as treatment for neuropathic pain, however side effects such as dry mouth, drowsiness, constipation, urinary retention and increased spasticity frequently occur (Cardenas et al., 2002; Rintala et al., 2007). Opioids, such as oxycodone and tramadol have also shown some efficacy as a medication for SCI-related neuropathic pain (Barrera-Chacon et al., 2011; Norrbrink & Lundeberg, 2009). In addition to the risk of dependence and abuse, constipation, nausea, and reduced cognitive function are side effects typical of opioids. These side effects negatively impact long-term use. Because neuropathic pain is difficult to effectively treat, multiple pharmaceuticals are often prescribed simultaneously. Increased dosages can further exacerbate side-effects. Thus, there is a need for alternative treatment methods.

One of the main challenges to developing sustainable, efficacious treatments for SCI-related neuropathic pain is the difficulty in determining the root cause of each individual's neuropathic pain. One potential cause is inflammation. SCI is commonly associated with immune impairment and many people with SCI are in a continual low-grade state of inflammation (Silva Alves et al., 2013). Inflammation is a precursor for many secondary health complications, including neuropathic pain. Neuropathy and SCI have been shown to cause an increase in proinflammatory cytokines TNF- α , IL-6 and IL-2, while anti-inflammatory cytokines IL-4 and IL-10 are reduced (Davies et al., 2007; Uceyler et al., 2007). Consistent exercise participation, however, has been shown to have an effect on the reduction of chronic low-grade inflammation (Petersen & Pedersen, 2005; Ford, 2002). Although exercise itself causes an acute inflammatory response, levels of proinflammatory cytokines are not increased. Cytokine IL-6, although commonly considered strictly pro-

inflammatory, contains anti-inflammatory properties as well, and increases in response to exercise (Petersen & Pedersen, 2005). This spike in IL-6 creates an anti-inflammatory environment by increasing the production of IL-10, IL-4 and IL-1RA (Petersen & Pedersen, 2005; Ford, 2002), while simultaneously inhibiting TNF- α production. The exercise-inflammation pathway has been well studied in the able-bodied population; however, research on this pathway in the SCI population has been limited. Further research is needed in the SCI population to determine if exercise can be utilized as an effective treatment to alter inflammation and decrease neuropathic pain.

1.3 Exercise and SCI-Related Neuropathic Pain

Exercise has been shown to have a plethora of psychological and physiological benefits in the SCI population (Devillard et al., 2007; Kehn & Kroll, 2009; Stevens et al., 2008) and may reduce the risk of some secondary health complications (Martin Ginis et al., 2012) including neuropathic pain (Ragnarsson, 1997). Indeed, self-report data indicate that some people with SCI use exercise to manage their neuropathic pain. Warms and colleagues (2002) conducted a two-sample postal survey of 471 persons with SCI and pain (musculoskeletal and neuropathic) to determine the frequency of use, and perceived efficacy of, various treatments. Nine individuals listed exercise as a mode of treatment and seven rated it to be extremely helpful. Perceived helpfulness of exercise was rated on a scale of 1-5, with sample 1 and 2 reporting a mean helpfulness score for exercise of 3.80, and 4.75, respectively. Although exercise was used by only a few respondents, the high helpfulness score suggests that for some people, exercise can be beneficial for alleviating pain.

Animal research suggests exercise can decrease neuropathic pain sensations. In a study by Hutchison et al., (2004), 39 rats were randomly assigned to a laminectomy control group, or they received a surgical SCI contusion. Rats with SCI were assigned to a treadmill training, swim training, stand training, or no training group. The exercise groups began their training at 4 days post-operation, and exercised for 20-25 minutes per day, 5 days per week for 7 weeks. Allodynia and hyperalgesia were tested using von Frey hairs applied to the plantar surface of the foot, and a finger pinch, respectively. Treadmill training led to a full recovery from allodynia, whereas the swim training group experienced a reduction in allodynia only to have it return by 28 days post-operation. Hyperalgesia was reduced in all exercise conditions compared with rats who did not receive exercise training. Overall, treadmill training (rhythmic and weight-bearing) showed the greatest efficacy as a treatment method for neuropathic pain, relative to the control group, however benefits were observed across all exercise groups.

To the best of our knowledge, only one study (Norrbrink et al., 2012) has looked at the effects of exercise training on neuropathic pain in humans with SCI. A 10-week, pre-post design, double-poling arm ergometer exercise programme was designed with the goal of decreasing neuropathic pain. Thirteen persons with paraplegia exercised 3 times per week, for 10 consecutive weeks. The exercise sessions lasted 50 minutes and consisted of alternating short (15s) and long (1-3m) intervals. Participants exercised at approximately 70-100% of their maximum heart rate. Pain was assessed using the International SCI Basic Pain Data Set questions, which measured pain localisation, type of pain, and pain intensity on a 0-10 numerical rating scale. In addition, pain interference was rated on a separate 0-6 numerical rating scale. Eight participants were administered pain questionnaires, as the

remaining five did not meet the required pain inclusion criteria for the study. These participants did not have pain present in one or more days during the previous week. Of these eight participants, seven indicated they had neuropathic pain and experienced a 2-point median reduction in pain intensity, with 6 of 10 pain locations decreasing by 1.8 clinically significant units. These results are similar to the amount of neuropathic pain symptom reduction resulting from pharmaceuticals (Guy et al., 2016), further supporting the utility of exercise as a treatment method for SCI-related neuropathic pain.

Taken together, these studies have shown exercise may be used as a treatment for SCI-related neuropathic pain reduction. However, many questions and gaps in the literature remain. Indeed, the clinicians and researchers who developed clinical practice guidelines for treatment of SCI-related neuropathic pain (Guy et al., 2016) have emphasized the need for further research on exercise as a treatment for neuropathic pain to address current limitations of the literature. Of the many limitations, three are pertinent to this thesis.

First, it is difficult to determine if exercise was efficacious in reducing overall pain, or specifically neuropathic pain. Different pain questionnaires were utilized within each study, leading to inconsistent measurement and identification of neuropathic pain. Second, it is unclear whether it was exercise participation in general, or the intensity of exercise in particular, that reduced SCI-related neuropathic pain. Participants in the study conducted by Norrbrink et al., (2012) exercised at 70-100% of their maximum heart rate, as opposed to the recommended 50-80% maximum heart rate (Martin Ginis et al., 2011), however this limitation will not be specifically addressed within this thesis. Third, diurnal fluctuations in neuropathic pain sensations of active individuals with SCI are important to observe to determine if, and how, neuropathic pain sensations change in response to exercise. No

study to date has examined the daily course of neuropathic pain in people with SCI and whether it is altered by exercise. Importantly, these limitations will be addressed by using a valid and reliable measure of neuropathic pain to assess individuals' naturalistic variations in pain over the course of a 6-day period and in response to exercise bouts.

1.4 Exercise, Pain and Affect in People with SCI

Affect is an instantaneous feeling of pleasure or displeasure (Ekkekakis, 2013) that lacks a cognitive component. Essentially, affect is how a person is generally feeling--positive or negative--at any given moment. In the general population, as well as those with rheumatoid arthritis, for example, research has shown that negative affect is also significantly correlated with self-reported pain (Hagglund et al., 1989; Smedstad et al., 1996) such that people who experience the most pain also experience the most negative affect. Furthermore, negative affect has been shown to modulate pain perception (Janssen, 2002). It is unclear, however, whether negative affect is related solely to the perception of pain, or whether it also alters the degree to which one responds to or experiences pain. Although research is inconclusive as to whether pain increases negative affect, or negative affect increases pain, it is clear that these two subjective experiences are related.

In the SCI population, people with higher pain levels have been shown to have more negative mood states (Rodrigues et al., 2013). This relationship has been further demonstrated by Cairns et al. (1996), and Jensen et al (2007), specifically regarding neuropathic pain sensations. Given that people who experience more negative affect also experience greater stress, negative mood, depression, and poorer overall psychological well-being (Dua, 1993), it is important to examine daily fluctuations in neuropathic pain

and affect in people with SCI to determine if a relationship exists. In addition, information on whether affect changes following a bout of exercise is potentially important for improving psychological well-being of individuals with SCI. Results from Martin Ginis and Latimer's (2007) study showed that bodily pain and affect improved following a single bout of body-weight supported treadmill training in adults with SCI. It is not clear, however, if the same effects hold for neuropathic pain and affect.

1.5 Purpose

Given the limitations of extant literature, coupled with the need to develop alternatives to pharmaceuticals to manage neuropathic pain experienced by persons with SCI, the present study was undertaken. The primary purpose was to observe how neuropathic pain sensations experienced by adults with SCI change in response to a bout of exercise. A secondary purpose was to determine if neuropathic pain and affective mood states are related in adults with SCI and if affect changes post-exercise. The third purpose of this study was to determine if there are associations between time of day, neuropathic pain and affect.

2 Hypotheses

2.1 Exercise and Neuropathic Pain

Hypothesis 1. Based on the results of the exercise intervention study conducted by Norrbrink and colleagues (2012) in which a reduction in perceived neuropathic pain was observed, in addition to the shared biological pathways between neuropathic pain and exercise in individuals with SCI (Allison, 2016), it is hypothesized that there will be an acute reduction in neuropathic pain sensations immediately following a bout of exercise.

2.2 Neuropathic Pain, Affect and Exercise

Hypothesis 2. Based on research showing correlations between affect and neuropathic pain in people with SCI (Cairns et al., 1996; Jensen et al., 2007), it is hypothesized that overall, fluctuations in affect will mirror fluctuations in pain, and affect will become more positive following exercise participation (Martin Ginis & Latimer, 2007).

2.3 Time of Day, Neuropathic Pain and Affect

Hypothesis 3. Given the absence of research observing fluctuations in neuropathic pain and affect in individuals with SCI at various time points per day, it was not possible to formulate a directional hypothesis. As a result, we tested the null hypothesis that there would be no correlation between neuropathic pain, affect, and time of day.

3 Methods

3.1 Design

This descriptive, observational study employed a case series design, and was determined to be feasible after the primary researcher engaged in multiple conversations with adults with SCI regarding the study design. Adults with SCI, who experience neuropathic pain sensations were followed over 6 days. With case series designs, participants are self-matched, therefore estimation is within-individuals and the design also controls for the risk of fixed confounders (such as age, years post injury, level of education). Utilizing a case series design allowed us to observe both the acute effects of exercise, and diurnal variations of neuropathic pain and affect within-individuals. This is advantageous because perception of neuropathic pain is a subjective, heterogeneous experience. Utilizing a study design where data are analyzed solely at the group level, may not reflect what is happening within-individuals.

Ecological momentary assessment (EMA) was built into the design of the study. EMA involves repeated sampling of participants' behaviours and experiences in real time and within their natural environments (Shiffman et al., 2008). Given that retrospective recall is subject to biases, and pain measured in a clinical setting may not be indicative of pain in an individual's natural environment (Rejeski et al., 1995), the ecological aspect of EMA can address these limitations. In this study, EMA was utilized in a randomized time-based manner and was conducted by prompting participants to complete assessments using a combination of interval-contingent and signal-contingent diaries. Interval-contingent diaries record measurements during a period of time (e.g., 6 days), which is divided into smaller intervals (e.g., 6 times per day; Thiele et al., 2002). Signal-contingent diaries rely

on measurements being recorded in response to a signal that occurs a fixed number of times per day on a random schedule (Moskowitz & Young, 2006). Using a combination of interval and signal-based measurements allowed participants to undertake their self-care routines without disruption by the study protocol while still maintaining the ecological element of randomized signals. Specifically, participants received one prompt within each interval at a time pre-determined by the researcher. These prompts were also scheduled to coincide as closely as possible with pre- and post- exercise. Smartphone software “mEMA by ilumivu” (Tuomenoksa, 2013) was utilized to deliver the prompts and collect the data.

3.2 Participants

There are no standardized guidelines for the number of cases to include in a case-series design. Published case series of individuals with SCI typically include 5-10 cases (Bani et al., 2015; Grassner et al., 2015; Jayaraman et al., 2007; Kumru et al., 2016; Pandey et al., 2016;). As such, six adults with SCI were recruited through advertisements emailed from community organizations from across Southern British Columbia. Individuals met the following inclusion criteria in order to be eligible for the study:

- a) have a spinal cord injury
- b) greater than 1 year post injury
- c) experience neuropathic pain sensations at- or below-level of injury
- d) participate in a structured exercise program, and meeting SCI Physical Activity Guidelines (Martin Ginis et al., 2011)
- e) have the ability to read and write English
- f) have access to a smartphone

Nine individuals volunteered to participate in this study and were screened to determine their eligibility. A total of 6 men met the inclusion criteria and participated in this study. They ranged in age from 27-50 years ($M = 39.33$, $SD = 8.24$). The University of British Columbia Okanagan Behavioural Research Ethics Board approved the study protocol. All participants provided written informed consent.

Table 1

Characteristics of the Study Participants

Participant	Gender	Time Since Injury	Injury Severity	Primary Mode of Mobility	Time Since Onset of NP (</>3months post injury)	Ethnicity	Medication for NP Relief	Marital Status
1	Male	6 years	Cervical, Incomplete	Manual Wheelchair	>3 months post injury	Caucasian	No	Single
2	Male	16 years	Cervical, Complete	Manual Wheelchair	<3 months post injury	Caucasian	No	Divorced
3	Male	16 years	Cervical, Incomplete	Power Wheelchair	>3 months post injury	Caucasian	Yes	Single
4	Male	10 years	Cervical, Incomplete	Manual Wheelchair	<3 months post injury	Caucasian	Yes	Single
5	Male	17 years	Cervical, Incomplete	Manual Wheelchair	<3 months post injury	Caucasian	Yes	Single
6	Male	9 years	Thoracic, Incomplete	Manual Wheelchair	<3 months post injury	Caucasian	Yes	Married

3.3 Apparatus

3.3.1 Physical Activity: Heart Rate Monitors

Fitbit Surge wrist-worn heart rate monitors were worn by participants to collect heart rate data that could be used to corroborate self-reported acute bouts of exercise. The timing of participants' elevated heart rate was matched to participant reports to ensure accuracy of self-reported exercise participation. Wrist-worn heart rate monitors were used as opposed to chest-worn monitors in order to alleviate the risk of skin breakdown for participants.

Fitbit Surge wrist-worn heart rate monitors have been tested in 15 manual wheelchair users (9 with SCI) against a validated, ActiHeart heart rate monitor and showed a strong correlation ($r=0.64$; $p<0.001$) (Tsang et al., 2016). However, the heart rate variations between monitors were larger when heart rate was greater than 100 bpm (i.e. during moderate to vigorous physical activity). Although moderate to vigorous physical activity may lead to slightly inaccurate heart rate measurements, Fitbit Surge wrist-worn heart rate monitors are strongly correlated with a validated heart rate monitor for manual wheelchair users. Therefore, they were utilized in this project to corroborate self-reported acute bouts of exercise.

3.3.2 Smartphone Software: mEMA

mEMA by ilumivu (Tuomenoksa, 2013) is designed for use on both Android and i-OS compatible software, and was utilized for data collection for this study. For each 6-day period of data collection, participants received six “real-time” push-prompts per day asking them to report their neuropathic pain and affect at a given moment in time. This allowed participants to receive notifications whether they were in internet range or not. Each participant was provided with a personalized code to enter into the app for the EMA prompts to be sent to their smartphones. Participants pressed send following completion of each neuropathic pain/affect survey block (each subset of 6 responses per day) which uploaded data to the central server.

3.4 Measures

3.4.1 Neuropathic Pain Scale

A modified version of Galer and Jensen's (1997) Neuropathic Pain Scale (NPS; Appendix A) was used to measure participants' neuropathic pain on both exercise and non-exercise days. This 10-item scale measures pain qualities typical of neuropathic pain. These include 'sharp', 'hot', 'dull', 'cold', 'sensitive', 'itchy', 'deep', and 'surface', in addition to two general qualities describing pain 'intensity' and overall pain 'unpleasantness.' The numerical rating scale ranges from (0) "Nothing at all" to (10) "the most intense sensation imaginable", for example. These assessed pain qualities have been deemed to be statistically different from one another (Galer & Jensen, 1997). One question regarding the temporal experience of neuropathic pain was excluded, due to the diurnal aspect of this study. The NPS has been validated among people with various neuropathic pain syndromes (including SCI) and has been shown to have the sensitivity to detect effects of treatment. As a result, previous research regarding potential pharmaceutical treatments for reducing neuropathic pain has shown that the NPS should be used in future studies to examine the effects of various treatments on the specific dimensions of neuropathic pain (Galer & Jensen, 1997).

3.4.2 Affect

Hardy and Rejeski's (1989) Feeling Scale (FS) was used in conjunction with Svebak & Murgatroyd's (1985) Felt Arousal Scale (FAS; Appendix A) to measure participants' affect and arousal in response to exercise and at various time points throughout the day. The FS is an 11-point, single item measure of pleasure-displeasure. The numerical rating scale

ranges from (-5) “Very Bad” to (+5) “Very Good”. A score of zero indicates neutral pleasure-displeasure. The FS has been established as a valid and reliable measure of exercise-related affective states (Hardy & Rejeski, 1989). The FAS, originally from the Telic State Measure, measures perceived activation and is a 6-point, single-item measure ranging from (1) “Low Arousal” to (6) “High Arousal.” The scale conceptualizes arousal as a measurement of how worked up an individual feels. For example, high arousal may include excitement, anxiety or anger, whereas low arousal may be relaxation, boredom or calmness. Using the FAS alongside the FS enhances construct validity by assessing activation in addition to valence (pleasure-displeasure; Watson & Clark, 1997).

Utilizing these measures of affect and arousal which incorporate different numerical rating scales will strengthen discriminant validity by having the respondent consider their answers for each specific scale (Ekkekakis, 2013). The FS and FAS have not been validated in the SCI population, however previous research suggests the FS is responsive to exercise participation of individuals with SCI (Martin Ginis & Latimer, 2007).

3.4.3 Physical Activity: PARA-SCI

The PARA-SCI (Martin Ginis et al., 2005) was utilized to identify when (time and day) people exercised and to corroborate heart rate data captured by the Fitbit Surge. Participants were interviewed via telephone regarding their physical activity over the previous 3 days. This standardized interview protocol occurred on Day 4 and Day 7 of the study. The PARA-SCI has been validated as a measure of physical activity among the SCI population in addition to having acceptable test-retest reliability. All three PARA-SCI

measures of total activity (cumulative, LTPA, lifestyle activity) have an intraclass correlation coefficient of >0.70 (Martin Ginis et al., 2005). This project utilized the PARASCI in combination with nightly participant check-ins and Fitbit Surge HR data to identify when participants completed bouts of exercise.

4 Protocol

Upon enrolment in the study, participants self-identified regarding the presence of neuropathic pain and completed a sociodemographic questionnaire (Appendix A). At this time, participants were asked which days and times they expected to exercise throughout the 6-day protocol which allowed the researcher to program mEMA with both randomized and accurately timed pre- and post-exercise prompts. This scheduling process ensured the participant received prompts pre- and post- exercise in addition to 4 other times per day. The researcher contacted the participant the evening prior to the anticipated exercise day to ensure their expected exercise time remained the same. The researcher minimized the risk of social desirability bias (Phillips & Clancy, 1972) by not informing the participants of the *specific* purpose of the study. Participants were only aware of the requirement of exercise participation. More specifically, they were not informed of the primary objective of the study being to observe changes in neuropathic pain from pre- to post-exercise. The researcher explained the study as an observation of neuropathic pain and affect fluctuations over the course of a typical day. As a result, participants were not answering survey prompts (specifically pre- and post- exercise) based on what they expected the desires of the researcher to be, but rather they answered them true to their current neuropathic pain sensations and core affect. While participating in the study, participants were instructed to maintain their usual activities. The order of administration of neuropathic pain and affect measures were systematically rotated to control for any order of presentation biases. Participants completed the questionnaires immediately before exercise, within 1 hour after exercise, as well as when mEMA prompts were received. Participants were instructed to have access to their devices from 9:00 AM to 9:00 PM to ensure rapid response times. A

total of 6 prompts per day, over the course of 6 days were sent to participants. Prompts were randomized within the following predetermined intervals:

Morning: (9:00 AM-11:00 AM)

Lunch: (11:01 AM-1:00 PM)

Early Afternoon: (1:01 PM-3:00 PM)

Evening: (3:01 PM-5:00 PM)

Late Evening: (5:01 PM-7:00 PM)

Night: (7:01 PM-9:00 PM)

Questionnaires were to be completed within a maximum of 15 minutes following the receipt of the mEMA prompt, before the application marked the data for the participant as missing. PARA-SCI was administered by the researcher on Days 4 and 7 of the protocol at a time agreed upon by participant and researcher. A structured, 4- question exit interview (Appendix A) was conducted in person by the researcher on Day 7 of the study protocol. This interview contained questions regarding topics such as the participant's perceptions of their neuropathic pain and affect fluctuations, and their experiences using mEMA. In addition, the researcher was available at all times of the study duration to assist with any potential technical difficulties, and to answer any questions.

5 Statistical Analyses

The number of measurement points for each participant ranged from 29-41, based on the number of answered prompts. Scores for NPS items were averaged to form a composite score based on each individual mEMA prompt. For example, if one item was not sent by mEMA due to technological errors, the NPS composite for that prompt would be based on an average score of 9 items rather than 10.

Data collected using mEMA at the time points immediately before and after exercise participation were analyzed at both the group level, and the individual level. At the group level, a paired samples t-test was conducted to test hypotheses one and two that neuropathic pain would decrease and positive affect would increase after exercise participation. T-tests were conducted for two bouts; exercise bout #1 refers to the first day of exercise within this study, and exercise bout #2 refers to the second day of exercise within this study. Assumptions of normality were tested using the Kolmogorov-Smirnov test. A two-tailed t-test was used with significance set at $p=0.05$.

Following each t-test, effect sizes were calculated using Laken's (2013) effect size calculator. Cohen's d_{av} was calculated using the equation $(M_{diff}/SD1+SD2/2)$. Hedge's g_{av} correction was applied ($Hg_{av} = SD1+SD2/2$) because Cohen's d_{av} is based on sample estimates and is positively biased (Lakens, 2013). Furthermore, when reporting effect sizes with a sample size of less than 20 individuals, Hedge's correction is more accurate than Cohen's d (Grissom & Kim, 2005). Using Hedge's correction permits reporting effect size estimates that are analogous across both within and between subject designs, therefore allowing for inclusion in future meta-analyses. Effect sizes were interpreted according to Cohen's (1988) conventions (small = 0.20, medium = 0.50, large = 0.80). In addition,

percentage pain change scores from pre-exercise to post-exercise for both exercise bouts were calculated using the equation $M_{\text{post}} - M_{\text{pre}} / M_{\text{pre}} \times 100$. A 30% reduction in pain intensity is considered to be clinically significant (Farrar et al., 2001), therefore this calculation was conducted to determine if exercise bout #1 or #2 led to a clinically significant reduction in neuropathic pain sensations.

At the individual level, data were plotted for each participant to examine changes from pre- to post-exercise. To display within-subject data, one graph was created per participant using GraphPad Prism 7.0 (2017). NPS, FS scores and FA scores were plotted on the y-axis and time of response was plotted on the x-axis. Plotting all variables on the same graph facilitated identification of patterns of change across measures.

The third hypothesis was tested at the intraindividual level. Bivariate Pearson's correlational analyses (Appendix B) were conducted in order to determine if correlations exist between time of day, neuropathic pain and affect. These analyses were conducted within-subjects because calculating correlations across all participants would violate the assumption of independence of observations (i.e. time of day data points are nested within participants).

Qualitative data analysis involved first transcribing structured interviews verbatim. Quotes were then extracted from transcripts that related to hypotheses #1, #2 or #3. Specifically, if participants spoke about either their neuropathic pain in response to exercise, their mood, or whether these constructs fluctuated throughout the day, these quotes were included. In the next section, qualitative data from each participant is presented along their respective quantitative results.

6 Results

6.1 Group Level Results

6.1.1 Neuropathic Pain

Descriptive statistics for neuropathic pain are presented in Table 2. For exercise bout #1, there was no significant difference between NP scores pre- and post- exercise. A small effect size was found ($Hg_{av}=0.18$), along with a -7.80% decrease in neuropathic pain sensations which is not considered clinically significant. For exercise bout #2, a significant difference between NP scores pre- and post- exercise was observed $t(5)=3.93$, $p=0.011$. NP scores decreased from pre- (3.02 ± 1.18) to post-exercise (2.42 ± 0.998), with a mean difference of (0.612 ± 0.38). A medium effect size ($Hg_{av}=0.52$) was found, in addition to a percentage change of -19.87% in neuropathic pain sensations, which was approaching clinical significance. These results partially support hypothesis #1, as neuropathic pain showed a reduction following participation in at least one bout of exercise.

6.1.2 Feeling Scale

Descriptive statistics for Feeling Scale scores are presented in Table 2. There was no significant difference between FS scores reported pre- and post- exercise for bout #1 or bout #2. A small effect size was found for FS scores pre- and post-exercise bout #1 ($Hg_{av}=0.22$). However, the effect size for FS scores pre- and post-exercise bout #2 ($Hg_{av}=0.76$) was medium to large. These results partially support hypothesis #2, as a large but non significant effect size was found for increased pleasure between pre- and post-exercise bout #2.

6.1.3 Felt Arousal

All Felt Arousal scores are presented in Table 2. There was no significant difference between pre- and post-exercise FA scores for bout #1 or #2. A very small effect size was found for both exercise bout #1 ($Hg_{av}=0.10$) and bout #2 ($Hg_{av}=0.11$). These results do not support hypothesis #2, as arousal did not significantly change following participation in exercise bout #1 or #2.

Table 2

Paired Samples T-Tests comparing NPS, FS and FA from Pre- to Post-Exercise (Bout #1 and Bout #2)

Pair	N	Mean	Standard Deviation	t	Sig.	95% Confidence Interval Lower	Upper
<i>Neuropathic Pain</i>							
Pre Exercise Bout #1 NP	6	2.95	1.22	0.882	0.418	-0.437	0.894
Post Exercise Bout #1 NP		2.72	1.24				
Pre Exercise Bout #2 NP	6	3.02	1.18	3.93	0.011	0.212	1.01
Post Exercise Bout #2 NP		2.41	1.00				
<i>Feeling Scale</i>						-1.60	0.938
Pre Exercise Bout #1 FS	6	2.833	1.17	-0.674	0.530		
Post Exercise Bout #1 FS		3.17	1.72				
Pre Exercise Bout #2 FS	6	2.17	1.72	-1.87	0.121	-3.17	0.504
Post Exercise Bout #2 FS		3.50	1.52				
<i>Felt Arousal</i>						-2.77	2.44
Pre Exercise Bout #1 FA	6	3.33	1.51	-0.164	0.876		
Post Exercise Bout #1 FA		3.50	1.64				
Pre Exercise Bout #2 FA	6	3.00	1.10	-0.237	0.822	-1.97	1.64
Post Exercise Bout #2 FA		3.17	1.83				

Note: NP = Neuropathic Pain. FS = Feeling Scale. FA = Felt Arousal.

6.2 Intraindividual Results

6.2.1 Participant 1

According to self-reported exercise participation captured by the PARA-SCI, participant #1 engaged in 90 minutes (60 minutes heavy, 30 minutes moderate) of bridging and isometric lower body resistance training for exercise bout #1. Exercise bout #2 consisted

of wheelchair treadmill training (25 minutes heavy, 10 minutes moderate, 5 minutes mild). Based on mEMA responses following exercise bout #1, participant #1 reported increased neuropathic pain sensations and displeasure but lower arousal. After exercise bout #2, he reported decreased neuropathic pain sensations, greater feelings of pleasure, but no change in arousal.

Significant positive correlations between NPS and FS scores ($r=0.480$, $p=0.007$), and NPS and FA scores ($r=0.610$, $p<0.001$) were observed. Time of day was significantly positively correlated with NPS ($r=0.623$, $p<0.001$), and FA scores ($r=0.449$, $p=0.013$), but not FS scores ($r=0.354$, $p=0.055$). These results suggest that as neuropathic pain increased, so did the state of arousal of participant #1. As time of day progressed, so did sensations of neuropathic pain and arousal (Table 3, Figure 1). The following quote from participant #1 supports the quantitative findings:

“My neuropathic pain increased the day after I performed lower body exercises, but I had minimal fluctuations after upper body exercise. I did not experience an increase in nerve pain at all, and I only experienced nerve pain from the waist down. Maybe belly button down. My upper body exercises did not increase neuropathic pain, but lower body did. Not directly following exercise – it was always delayed by 12-24 hours. Immediately following exercise my neuropathic pain did not increase.”

Taken together, for participant #1, these results support hypothesis #2 as changes in neuropathic pain were mirrored by changes in affect. Furthermore, these results suggest null hypothesis #3 be partially supported; although time of day was significantly correlated with neuropathic pain and arousal, time of day was not significantly correlated with

feelings of pleasure/displeasure.

Table 3

Intraindividual Correlations: Participant 1^a

	Neuropathic Pain	Feeling Scale	Felt Arousal	Time of Day
Neuropathic Pain Scale	--	r=0.480** p=0.007	r=0.610** p<0.001	r=0.623** p<0.001
Feeling Scale	--	--	r=0.864** p=0.000	r=0.354 p=0.055
Felt Arousal	--	--	--	r=0.449* p=0.013

^a. Data points = 30

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

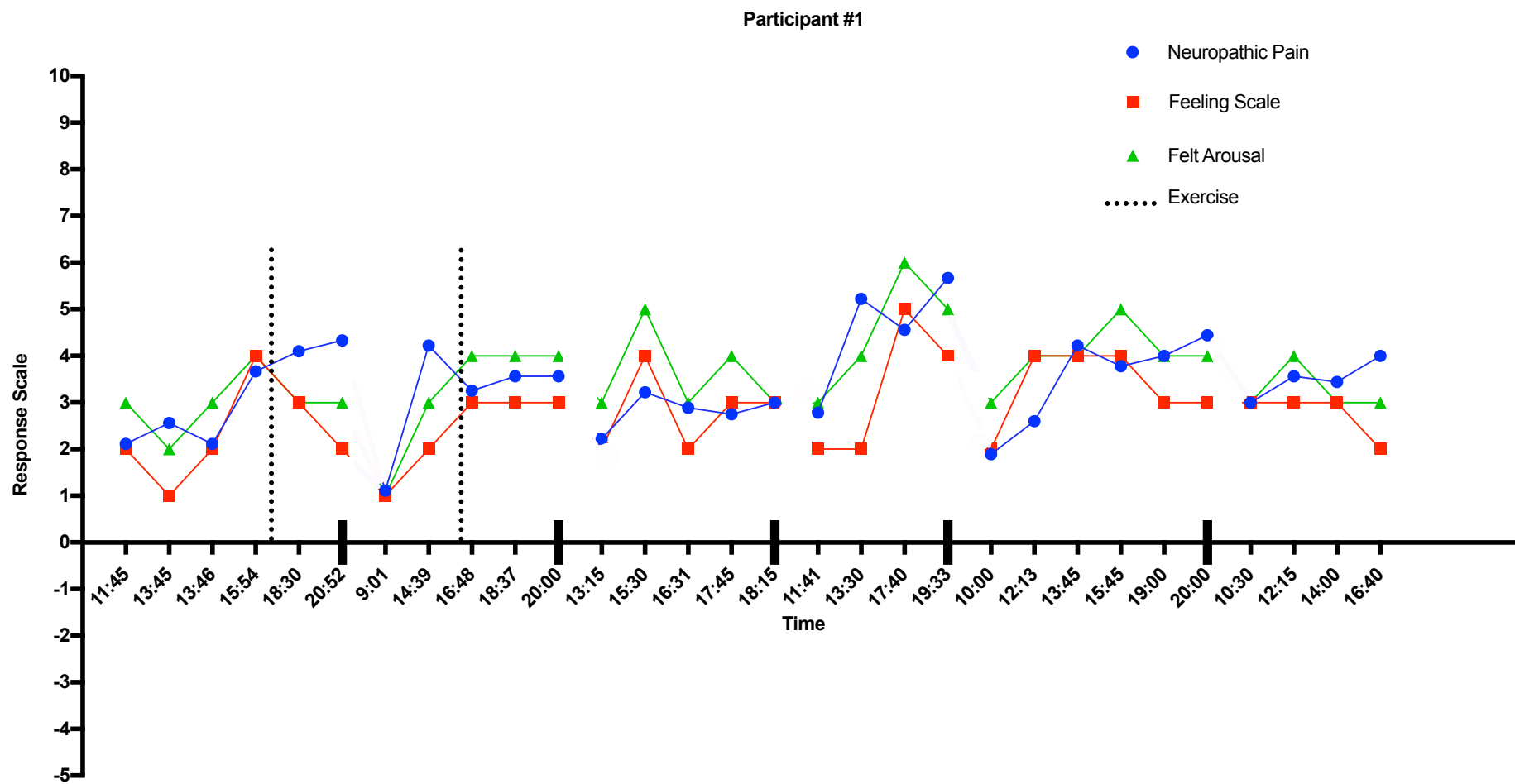


Figure 1: Diurnal Variations in NP, FS, FA: Participant 1

6.2.2 Participant 2

Participant #2 engaged in 90 minutes of heavy intensity hand cycling for exercise bout #1, and 90 minutes of heavy intensity upper-body resistance training for exercise bout #2, according to data captured by the PARA-SCI. Based on mEMA responses, participant #2 experienced a decrease in neuropathic pain sensations and increased feelings of pleasure but no changes in arousal following both exercise bouts #1 and #2.

NPS was significantly, negatively correlated with FS scores ($r=-0.580$, $p<0.001$), but not FA scores ($r=0.121$, $p=0.495$). Time of day was not significantly correlated with NPS ($r=0.019$, $p=0.915$), FS scores ($r=-0.047$, $p=0.793$), or FA scores ($r=0.180$, $p=0.309$). These results suggest that as neuropathic pain experienced by participant #2 increased, their feelings of displeasure increased but arousal was not affected. Furthermore, time of day was not related to neuropathic pain, feelings of pleasure/displeasure, or arousal of participant #2 (Table 4, Figure 2).

Personal experiences of participant #2 partially support his quantitative results:

“Yeah- hopefully it will be reflected in what I put in, but there were definitely certain times in the day that it was more acute, like I said, in the morning it was fairly nonexistent. At different times of the day, and different times it [this methodology] brought it [neuropathic pain sensations] to the forefront- It made me more aware of what was going on in my feet, right[...] I don’t know if physiologically, whether the exercise umm, lessens it or whether you are so preoccupied that you are just not thinking of it anymore. I don’t know if I could make any connections that way.”

In combination, these results partially support hypothesis #2, as his neuropathic pain

sensations were mirrored by changes in his feelings of displeasure, but not arousal. Null hypothesis #3 may be partially supported as participant #2's subjective experience suggest that time of day had an effect on neuropathic pain, however this was not reflected in the quantitative data.

Table 4

Intraindividual Correlations: Participant 2^b

	Neuropathic Pain	Feeling Scale	Felt Arousal	Time of Day
Neuropathic Pain Scale	--	r=-0.580** p<0.001	r=0.121 p=0.495	r=0.019 p=0.915
Feeling Scale	--	--	r=0.129 p=0.468	r=-0.047 p=0.793
Felt Arousal	--	--	--	r=0.180 p=0.309

^b Data points= 34

** Correlation is significant at the 0.01 level (2-tailed)

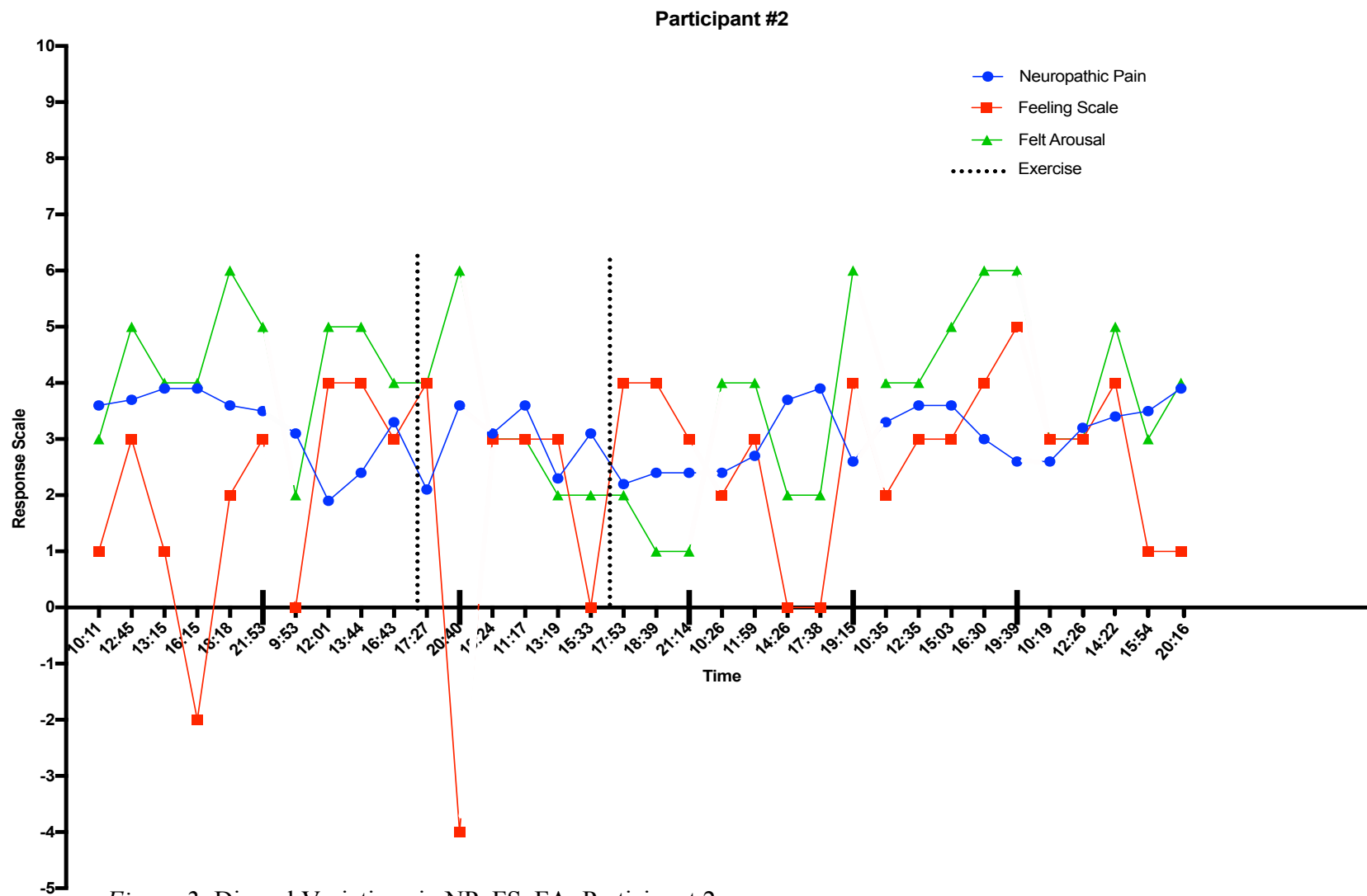


Figure 2: Diurnal Variations in NP, FS, FA: Participant 2

6.2.3 Participant 3

Self-reported activity captured by the PARA SCI indicates that for exercise bout #1, participant #3 engaged in a combination of resistance and aerobic training. He began with 15 minutes of moderate resistance training, 10 minutes of cardio/ball toss at a heavy intensity, 6 upper body pulley exercises for 60 minutes working at a heavy intensity, and finished with 20 minutes of moderate intensity stretching. Participant #3 played wheelchair rugby for exercise bout #2, which included 55 minutes of moderate intensity, 50 minutes of heavy intensity, and 10 minutes of mild intensity. This exercise bout ended with 400 meter indoor, wheeling time trials, which required 4 minutes of heavy intensity activity. According to mEMA responses, following exercise bout #1, a slight decrease in neuropathic pain sensations and a notable increase in overall affect was experienced by participant #3. Exercise bout #2 led to a slight decrease in neuropathic pain sensations, and increased feelings of pleasure and arousal.

NPS was not significantly correlated with FS scores ($r=0.255$, $p=0.139$) or FA scores ($r=0.241$, $p=0.163$). Time of day, however, was significantly positively correlated with NPS ($r=0.352$, $p=0.038$), FS scores ($r=0.507$, $p=0.002$), and FA scores ($r=0.463$, $p=0.005$). These results suggest that neuropathic pain, feelings of pleasure, and arousal of participant #3 increased as time of day progressed (Table 5, Figure 3). Experiences of participant #3 support hypothesis #1:

“After workouts, it seemed like it calmed the pain down some, but it may have just been my mind being taken off of the pain, and not really thinking about it. If that makes sense [...] I think the more I got my blood flowing, it seemed that the sensation was more just of a buzzing, but the more relaxed and sitting around I

was, the more I would feel fiery and zapping pain. Just zaps going out. That's how I would describe it."

Taken together, participant #3's results support hypothesis #1 because neuropathic pain decreased following exercise participation. These results reject hypothesis #2 because feelings of pleasure/displeasure and arousal did not align with changes in neuropathic pain experienced. Furthermore, these results reject null hypothesis #3 because time of day was related to neuropathic pain and affect of participant #3.

Table 5

Intraindividual Correlations: Participant 3^c

	Neuropathic Pain	Feeling Scale	Felt Arousal	Time of Day
Neuropathic Pain Scale	--	r=0.255 p=0.139	r=0.241 p=0.163	r=0.352* p=0.038
Feeling Scale	--	--	r=0.560** p<0.001	r=0.507** p=0.002
Felt Arousal	--	--	--	r=0.463** p=0.005

^a Data points= 35

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

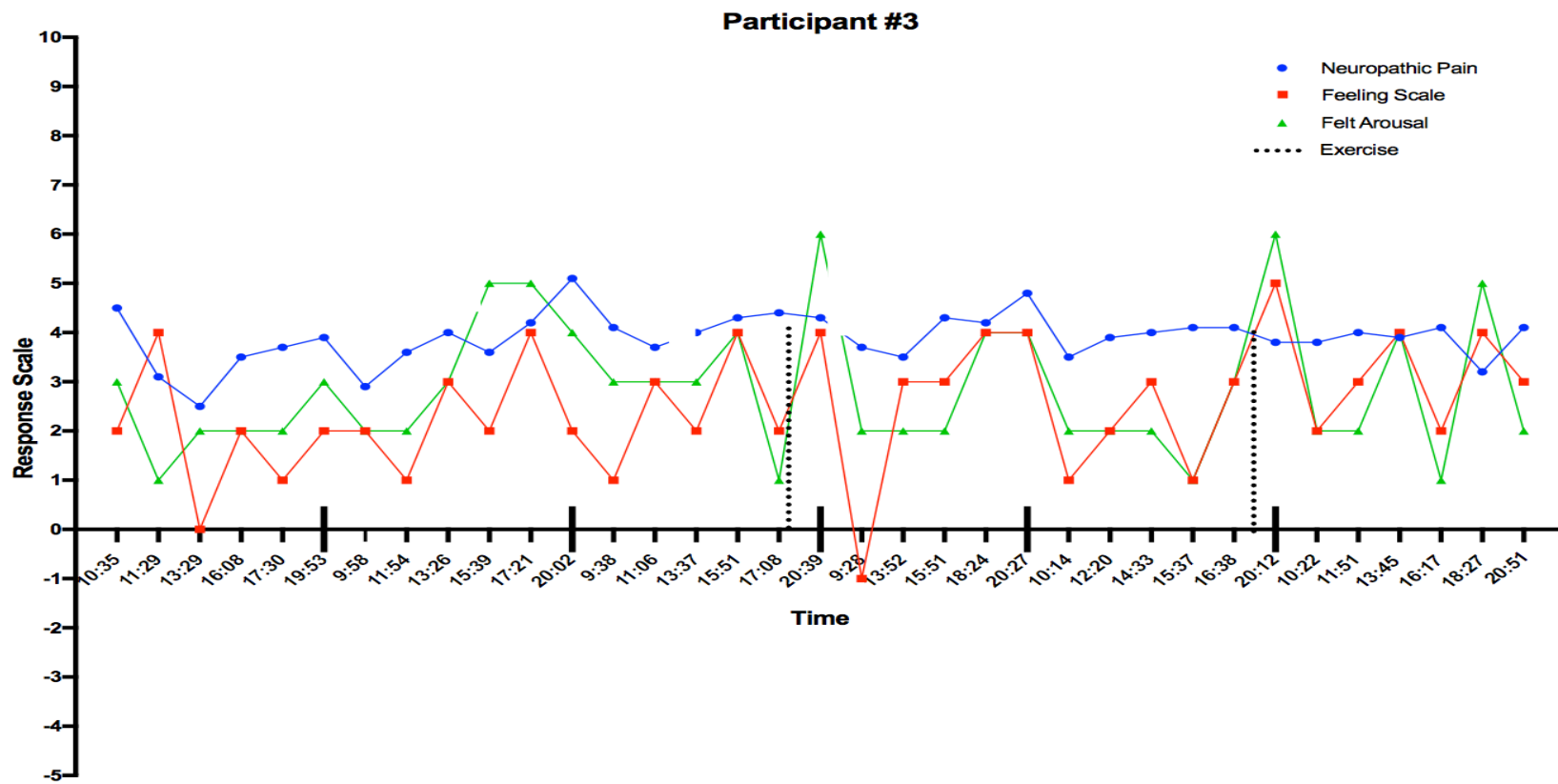


Figure 3: Diurnal Variations in NP, FS, FA: Participant 3

6.2.4 Participant 4

Participant #4 participated in wheelchair basketball for exercise bout #1, which consisted of 10 minutes of mild activity, 20 minutes of moderate activity, and 10 minutes of heavy activity, according to data captured by the PARA-SCI. Exercise bout #2 involved participation in 90 minutes of wheelchair curling (70 minutes moderate, 20 minutes mild). Based on mEMA responses, following exercise bout #1, participant #4 experienced decreased neuropathic pain sensations and increased feelings of pleasure and arousal. He reported decreased neuropathic pain sensations and levels of arousal, with no change in feelings of pleasure/displeasure after exercise bout #2.

NPS was not significantly correlated with FS scores ($r=-0.009$, $p=0.955$) or FA scores ($r=-0.251$, $p=0.114$). Furthermore, time of day was not significantly correlated with NPS ($r=-0.242$, $p=0.127$), FS scores ($r=-0.008$, $p=0.959$), or FA scores ($r=0.072$, $p=0.653$). These results suggest that neuropathic pain sensations and overall affect of participant #4 were not related. In addition, time of day did not play a role in the sensations of neuropathic pain experienced by participant #4, or his affect (Table 6, Figure 4). Participant #4's self-reported experiences partially contradict his quantitative data:

“Mornings and laziness causes a lot more stiffness and burning. My legs would feel like they are on fire, at the bone, but my hands can be itchy and cold. You can have a warm, burning sensation deep in your legs but a surface, itchy feeling on your arms. I’ve never really thought about it before, because you get used to it. I try not to pay attention to it.”

Taken together, for participant #4, these results reject hypothesis #2 because changes in neuropathic pain were not mirrored by changes in feelings of pleasure/displeasure or arousal. These results partially support null hypothesis #3 because

qualitative reports suggest that time of day was related to changes in neuropathic pain and affect, however this was not reflected quantitatively.

Table 6

Intraindividual Correlations: Participant 4^d

	Neuropathic Pain	Feeling Scale	Felt Arousal	Time of Day
Neuropathic Pain Scale	--	r= -0.009 p= 0.955	r= -0.251 p= 0.114	r= -0.242 p= 0.127
Feeling Scale	--	--	r=0.456** p=0.003	r= -0.008 p= 0.959
Felt Arousal	--	--	--	r= 0.072 p= 0.653

^d. Data points= 41

** Correlation is significant at the 0.01 level (2-tailed)

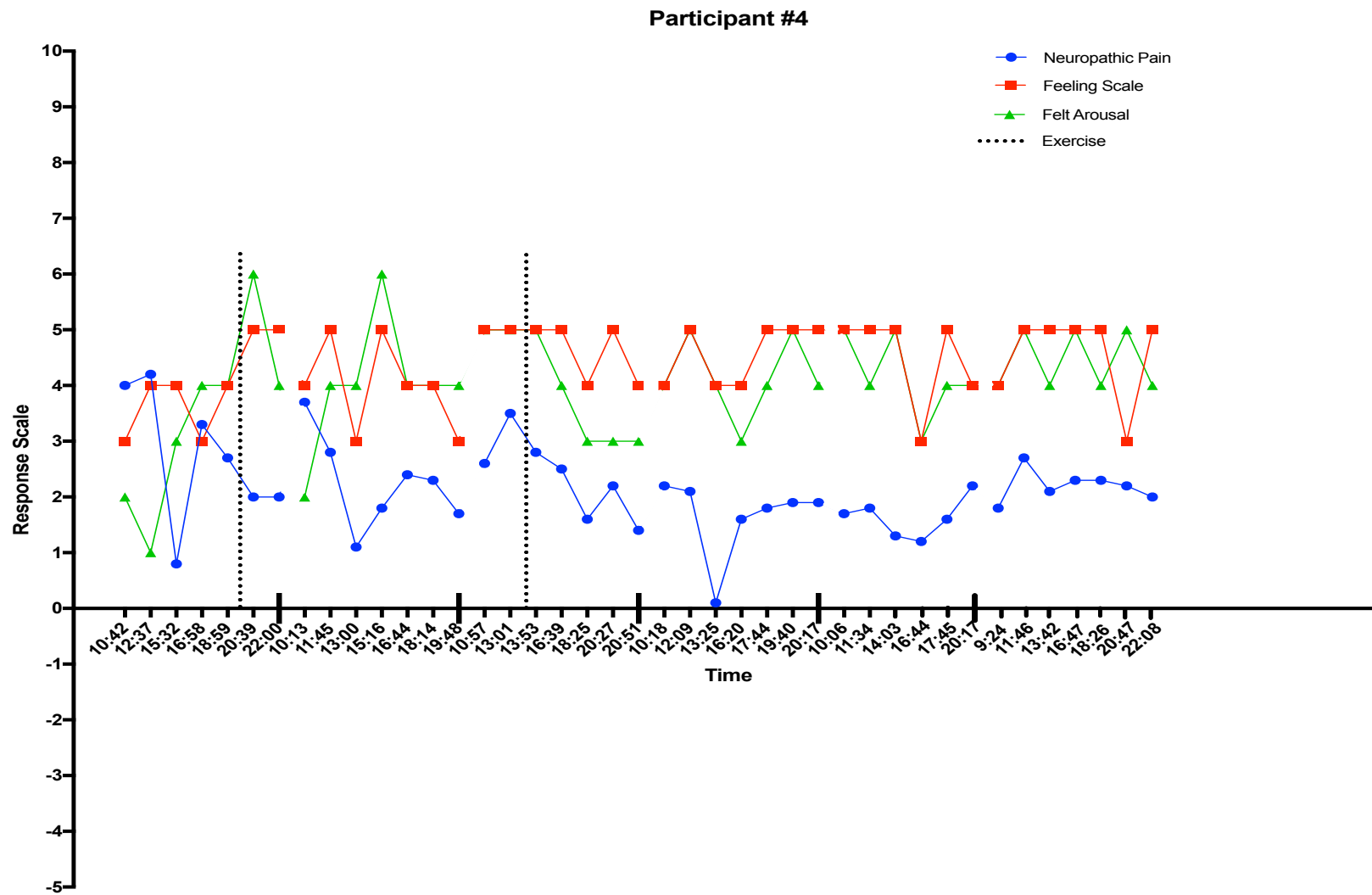


Figure 4: Diurnal Variations in NP, FS, FA: Participant 4

6.2.5 Participant 5

Participant #5 engaged in indoor wheeling on a rubber track for both exercise bout #1 and bout #2, however exercise bout #1 was 30 minutes of heavy activity, while exercise bout #2 was 25 minutes of heavy activity and 20 minutes of moderate activity. According to mEMA responses, following exercise bout #1, participant #5 experienced an increase in neuropathic pain sensations, decreased arousal but no changes in feelings of pleasure/displeasure. He reported decreased neuropathic pain sensations, greater displeasure and decreased arousal following exercise bout #2.

NPS was not significantly correlated with FS scores ($r=-0.097$, $p=0.572$), or FA scores ($r=0.216$, $p=0.206$). No significant correlations were found between time of day and NPS ($r=-0.094$, $p=0.596$), FS scores ($r=-0.129$, $p=0.453$), or FA scores ($r=-0.220$, $p=0.197$) (Table 7, Figure 5). These results suggest that neuropathic pain and overall affect were not related for participant #5. Furthermore, neuropathic pain, feelings of pleasure/displeasure, and arousal did not change based on time of day. Participant #5 reported experiences that partially differed from his quantitative results:

“I found that it [neuropathic pain] changed while I was- when my mind was present on something else. After a wheel- and I am in a meditative area- from a mental standpoint I felt my pain was less. Not sure if it’s a physical standpoint. I noticed more and more how random my nerve pain is.”

Taken together, these results reject hypothesis #2, because changes in neuropathic pain did not align with changes in feelings of pleasure/displeasure or arousal for participant #5. These results support null hypothesis #3 as time of day was not related to neuropathic pain or affect of participant #5.

Table 7*Intraindividual Correlations: Participant 5^e*

	Neuropathic Pain	Feeling Scale	Felt Arousal	Time of Day
Neuropathic Pain Scale	--	r= -0.097 p=0.572	r= 0.216 p= 0.206	r= -0.094 p= 0.586
Feeling Scale	--	--	r= 0.342* p=0.041	r= -0.129 p=0.453
Felt Arousal	--	--	--	r= -0.220 p=0.197

^e. Data points= 36

* Correlation is significant at the 0.05 level (2-tailed)

Participant #5

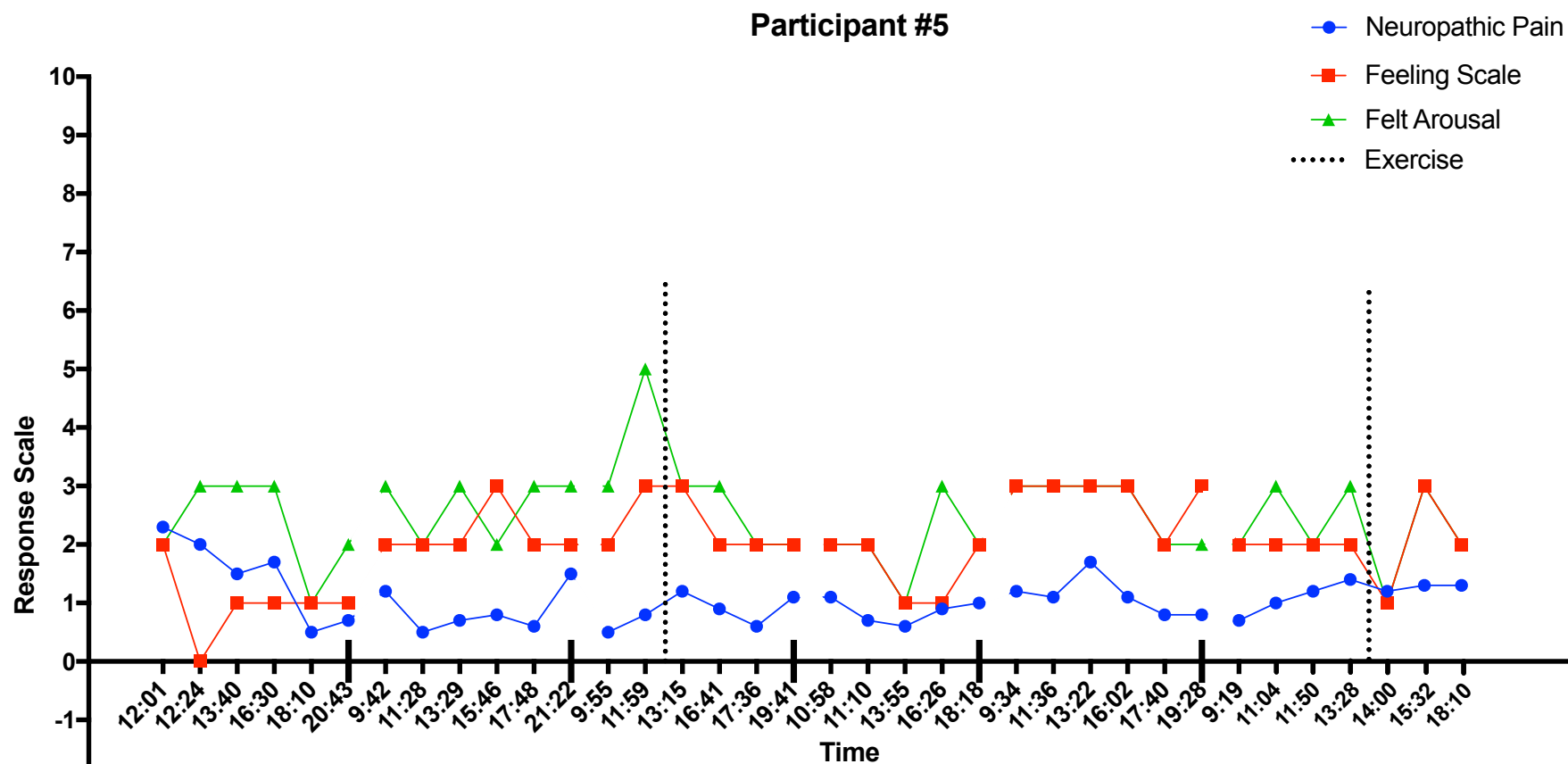


Figure 5: Diurnal Variations in NP, FS, FA: Participant 5

6.2.6 Participant 6

Participant #6 performed a standing and lowering exercise routine while wearing leg braces for both exercise bout #1 and bout #2. Each bout was performed for 30 minutes, with bout #1 being performed at a moderate intensity, while bout #2 was performed at a mild intensity. According to mEMA responses, participant #6 experienced a decrease in neuropathic pain sensations following both exercise bouts within this study. Following exercise bout #1, participant #6 experienced a slight increase in displeasure and a slightly decreased state of arousal. He experienced an increased feeling of pleasure with no changes in arousal following exercise bout #2.

NPS was not significantly correlated with FS scores ($r=-0.107$, $p=0.581$) or FA scores ($r=0.177$, $p=0.358$). Time of day was not significantly correlated with NPS ($r=-0.244$, $p=0.202$), FS scores ($r=0.188$, $p=0.329$), or FA scores ($r=-0.332$, $p=0.079$). These results suggest that neuropathic pain sensations, feelings of pleasure/displeasure, and arousal experienced by participant #6 were not related. Furthermore, these constructs did not change based on time of day (Table 8, Figure 6). Participant #6 reported experiences that align with hypothesis #1:

“Yes. After working out [standing and lowering] I noticed the pain did go down.

And after doing numerous transfers, the pain would go up.”

In combination, these results reject hypothesis #2, as changes in neuropathic pain did not mirror changes in affect. These results support null hypothesis #3, as time of day did not significantly relate to neuropathic pain or affect of participant #6.

Table 8*Intraindividual Correlations: Participant 6^f*

	Neuropathic Pain	Feeling Scale	Felt Arousal	Time of Day
Neuropathic Pain Scale	--	r= -0.107 p=0.581	r= 0.177 p=0.358	r= -0.244 p=0.202
Feeling Scale	--	--	r= 0.344 p=0.068	r= 0.188 p=0.329
Felt Arousal	--	--	--	r= -0.332 p=0.079

^f. Data points=29

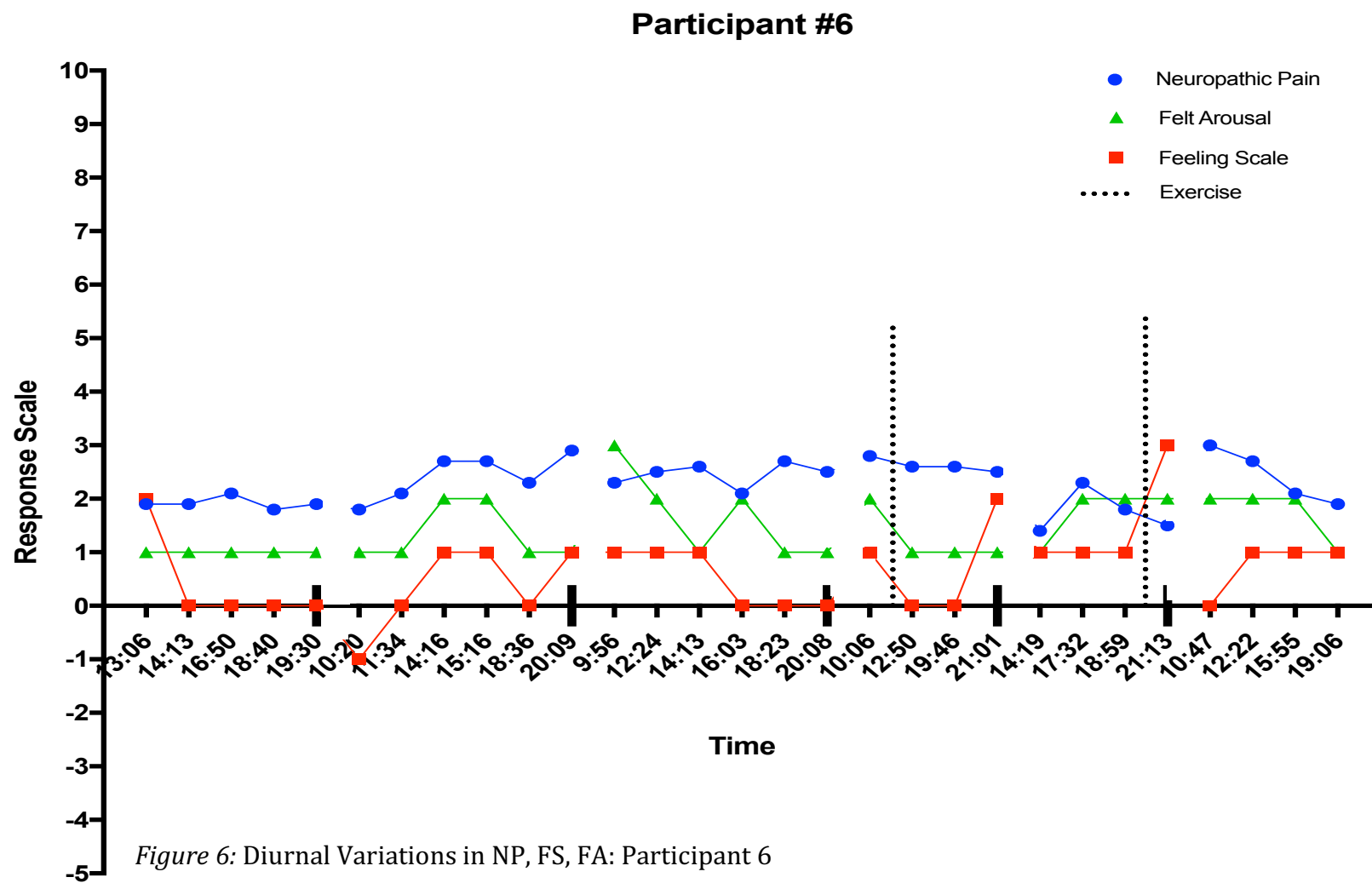


Figure 6: Diurnal Variations in NP, FS, FA: Participant 6

6.3 Results Summary

The following is a summary of both group level and intraindividual results from this thesis study. The summary is based on quantitative and qualitative data.

Table 9

Summary of Group Level and Within-Subject Results (Quantitative and Qualitative)

	Group Level	Within Subjects					
		S1	S2	S3	S4	S5	S6
Hypothesis 1	Partial Support	P	√	√	√	P	√
Hypothesis 2	Partial Support	P	√	√	P	×	P
Hypothesis 3	Not Applicable	P	√	×	P	√	√

Note: P= partial support of hypothesis. × = fail to support hypothesis. √= supports hypothesis

Hypothesis 1. It was hypothesized that a reduction in neuropathic pain sensations will occur following exercise. At the group level, this hypothesis was partially supported. This conclusion is based on the significant reduction in neuropathic pain sensations occurring following exercise bout #2, but not bout #1. At a within-subjects level, 4 out of 6 participants experienced a decrease in neuropathic pain following both exercise bouts and 2 experienced a decrease in their neuropathic pain sensations following exercise bout #2, but had increased neuropathic pain following bout #1.

Hypothesis 2. Overall, fluctuations in neuropathic pain and affect were hypothesized to mirror each other, with affect becoming more positive following exercise participation. This hypothesis was partially supported at the group level. Two out of 6 participants experienced more positive affect following both exercise bouts, whereas 3 participants experienced greater positive affect following only one exercise bout. One participant experienced greater negative affect following

both exercise bouts.

Hypothesis 3. The null hypothesis that no correlation would be present between time of day, neuropathic pain and affect was supported by 3 out of 6 participants. Results from 2 participants partially supported this hypothesis, due to either conflicting qualitative and quantitative data, or significant correlations existing between certain constructs but not all. One participant's results rejected the null hypothesis, as he had a significant correlation between time of day, neuropathic pain and affect.

No adverse events were reported by participants regarding their participation in the study protocol.

7 Discussion

The primary purpose of this study was to observe how neuropathic pain sensations experienced by adults with SCI change in response to a bout of exercise. A secondary purpose was to determine if neuropathic pain and affective mood states are related in adults with SCI. The third purpose of this study was to determine if there are associations between time of day, neuropathic pain and affect. The primary finding of the present study was that neuropathic pain may be reduced following exercise participation, and some individuals may also experience a simultaneous increase in positive affect. In addition, as time of day progresses, some adults with SCI may experience increases in their neuropathic pain and negative affect. To the best of our knowledge, this is the first study to evaluate the effect of exercise on both neuropathic pain and affective mood states of adults with SCI. Furthermore, this study provides an initial contribution to the scientific literature regarding diurnal variations in neuropathic pain sensations and affect in adults with SCI.

7.1 Exercise and Neuropathic Pain

In partial support of hypothesis one, neuropathic pain sensations were reduced for all participants following at least one bout of exercise. These findings align with previous research, which found a 10-week exercise training intervention led to a median neuropathic pain intensity reduction of 2 units on a 0-10 numerical rating scale (Norrbrink et al., 2012). Furthermore, two studies have shown treadmill training to be efficacious in reducing neuropathic pain manifestations (i.e. allodynia and tactile hypersensitivity) in animal models (Hutchison et al., 2004; Stagg et al., 2011). However, these studies did not evaluate the acute effect of exercise on neuropathic pain sensations, nor did they observe changes in neuropathic pain over the course of the day. Our study is the first to evaluate the acute effects of exercise on neuropathic pain in adults with SCI, within the context of a typical day.

One reason why exercise may reduce neuropathic pain sensations in persons with SCI is due to the role of inflammation. Individuals with SCI who experience neuropathic pain sensations have been shown to have higher levels of inflammatory cytokines IL-6 and TNF- α compared with those who do not experience neuropathic pain (Davies et al., 2007). Leukocytes secrete cytokines (such as IL-6), but contracting skeletal muscle is also a major producer. In the general population, Steensberg and colleagues (2000) have shown that an experimental increase in IL-6, similar to levels released by skeletal muscles during exercise, induces an anti-inflammatory response by increasing the production of anti-inflammatory cytokines IL-1RA and IL-10. The levels of IL-6 production, and the resultant increase in IL-1RA and IL-10, are strongly dependent on exercise intensity and the amount of muscle mass engaged. As a result, it is not well understood whether strictly upper body exercises will require large enough musculature to evoke this anti-inflammatory response (Pedersen & Febbraio, 2008). It is also important to consider the duration of exercise participation, as longer lasting activities result in higher IL-6 production. Cytokine levels were not measured within this current study; therefore, this explanation is entirely speculative. However, further research regarding the anti-inflammatory effect of exercise is necessary--specifically in regards to the role of exercise intensity and duration.

One other explanation for exercise leading to a reduction in neuropathic pain sensations may be due to the phenomenon known as exercise induced analgesia (EIA). In the general population, EIA has been increasingly evaluated in recent years. EIA can be understood as engaging in strenuous exercise in the presence of severe pain, and later reporting lower levels of/complete elimination of pain (Padawer & Levine, 1992). This has led to the hypothesis that exercise can increase one's pain tolerance. What has also been observed, however, is that there are thresholds for both the intensity and duration of exercise required to elicit EIA (Hoffman et al., 2004).

Although objective measurements of intensity and exact durations of exercise were not collected within this study, these training parameters may be important for observing changes in SCI-related neuropathic pain (Norrbrink et al., 2012). It is possible that greater durations or higher intensities of exercise may have facilitated the changes in neuropathic pain sensations in response to exercise participation.

An interesting question, however, is why some people responded to exercise and others did not. Ditor and colleagues (2005) defined exercise responders with SCI in their bodyweight supported treadmill training program as those who experienced an average exercising heart rate of greater than 100 beats per minute, whereas non-responders did not meet this heart-rate threshold. This threshold might explain why Norrbrink and colleagues (2012) showed support for the importance of exercise intensity in reducing neuropathic pain sensations, as participants in their study were working at 70-100% HR max, which was above the previously suggested HR max of 50-80% (Martin Ginis et al., 2011). Perhaps people need to achieve this intensity threshold during exercise to decrease neuropathic pain. However, given the impaired heart rate response to exercise that occurs as a consequence of SCI, not all participants may be able to achieve this level of exercise intensity. Sympathetic hypoactivity occurs as a result of interrupted descendent pathways following SCI. Among other cardiac adaptations, sympathetic hypoactivity results in low heart rate, reflex bradycardia, and low resting blood pressure (Grigorean et al., 2009). Cardiac sympathetic impulses initiate at T1-T4 spinal segments; thus, individuals with cervical and high-thoracic SCI have impaired spinal sympathetic innervation. For some individuals with SCI, achieving a HR of 100 BPM, even during high-intensity exercise participation, may not be possible. Therefore, an individual's function and degree of autonomic control may play a prominent role in determining whether they experience a decrease in neuropathic pain in response

to exercise. It is important to recognize that it may be individual characteristics (e.g., injury level, completeness), rather than characteristics of exercise that dictate responsiveness.

In addition to exercise intensity influencing pain responsiveness, exercise type may also be important. Qualitative data suggest that engaging in certain exercises led to greater neuropathic pain reduction compared to other exercises. For example, Participant #1 stated: *“My neuropathic pain increased after I performed lower body exercises, but I had minimal fluctuations after upper body exercises. Yeah, no increased nerve pain at all. I only experience nerve pain from the waist down, maybe belly button down. But yeah, upper body exercises don’t increase my nerve pain, but lower body exercises like bridging did increase nerve pain in lower body.”* The heterogeneity of neuropathic pain responses to exercise is displayed when comparing Participant #1 with Participant #6. *“After working out, which was standing and lowering, I noticed the nerve pain did go down. And after doing numerous transfers, the pain would go up.”* For participant #1, lower body exercises increased his neuropathic pain, whereas for participant #6, they decreased his neuropathic pain. Determining how different exercise protocols, in terms of intensity and type, influence individual neuropathic pain responses to exercise training is an important area of research to target.

7.2 Exercise, Pain and Affect

At the group level, increased feelings of pleasure occurred from pre-exercise to post-exercise bout #2, but not exercise bout #1, which partially supports hypothesis #2. Research is very limited regarding the interrelationship between exercise, feeling states, and pain experienced by individuals with SCI. For other chronic disability populations, such as people with knee osteoarthritis, studies have reported relationships between these variables. Focht and colleagues

(2002; 2004), for instance, conducted a study utilizing EMA to observe the influence of diurnal variations, stress, and pain on daily feeling states of sedentary, older adults with knee osteoarthritis. In addition, they aimed to determine if acute exercise contributed to fluctuations in momentary feeling states. Their results showed that acute exercise led to increased pain perceptions when compared with measures of pain taken at the same time of day on a day without exercise. Furthermore, exercise participation did not induce a significant post-exercise improvement in feeling states.

In a sample of people with SCI, Martin Ginis and Latimer (2007) conducted a pre-test, post-test bodyweight supported treadmill training study to determine whether exercise-related changes in feeling states were related to exercise-related changes in pain and in-task pain. Overall, results showed that exercise-related changes in pain were significantly, negatively correlated with changes in feeling states which indicated that as pain decreased, feelings of pleasure increased. Taken together, these contrasting results suggest that acute changes in neuropathic pain and feeling states in response to exercise may vary between chronic disability populations, such as those with SCI and knee osteoarthritis.

This finding is perhaps not surprising, given root physiological causes of pain sensations are assumed to be different between SCI-related neuropathic pain and osteoarthritic knee pain. One reason for these differential findings of Focht et al., (2004) and Martin Ginis and Latimer (2007) may be that exercise exacerbates pain for individuals with knee osteoarthritis, but does not increase neuropathic pain experienced by adults with SCI. Results from the current study support the findings of Martin Ginis and Latimer (2007), which provides further evidence that acute feelings of pleasure may be related to exercise participation and reduced levels of pain for individuals with SCI. It is also of interest for future investigations to determine whether these

affective responses vary based on the type, duration, or intensity of exercise participation.

7.3 Neuropathic Pain, Affect and Time of Day

The null hypothesis that no correlation would exist between time of day, neuropathic pain and affect was partially supported. Participants had conflicting quantitative and qualitative results for this hypothesis, and one individual had a significant, positive correlation between all of these outcome variables.

To the best of our knowledge, only one other study has examined momentary aspects of pain in the SCI population. Kratz and colleagues (2017) utilized EMA and end-of-day diaries to observe whether pain acceptance moderates the momentary associations of pain intensity with pain interference and physical activity in people with chronic pain and SCI. The EMA protocol was interval-contingent, and participant responses occurred 5 times per day, over 7 consecutive days (in addition to participants filling out online end-of-day diaries.) Average physical activity counts per minute were calculated for each interval, and matched to the time of prompt response. Kratz et al (2017) did not look explicitly at neuropathic pain, but rather diurnal variations in chronic pain. Results showed a significant linear diurnal pattern for momentary pain ratings ($B=0.11$, $p=0.004$), with pain steadily increasing from wake until 7 PM, and then slightly decreasing before bedtime.

Based on the quantitative data, 2 participants showed this pattern in our study. A temporal pattern in neuropathic pain intensity has also been shown in two studies involving individuals who suffer from painful diabetic neuropathy and postherpetic neuralgia (Gilron et al., 2013; Odrich et al., 2006). Results from these studies suggest that neuropathic pain intensity increases throughout the day from 8:00 AM to 8:00 PM. In contrast to these studies, our results align with the case series conducted by Strian et al (1988), who demonstrated that some individuals exhibited a temporal

pattern in their pain intensities, but others did not.

Overall, results from this study support general findings that diurnal patterns exist between time of day, neuropathic pain and affect, but these relationships are inconsistent across participants. For a majority of participants within this study, time of day was significantly correlated with neuropathic pain sensations, however the direction of these correlations varied. For example, participant #2 reported, *“Yeah[...] there were definitely certain times in the day that it was more acute, like I said, in the morning it was fairly nonexistent”* whereas participant #4 stated, *“Yeah. Mornings and laziness caused a lot more stiffness and burning.”*

One reason for neuropathic pain worsening (for some participants) as the time of day progresses may be due to the reduction of mental stimulation at nighttime. More distractions are present during the day for majority of individuals, which may inhibit neuropathic pain from being the most prominent thought in the minds of those who experience it. For example, participant #3 reported, *“At the times, when I was occupying my brain, it didn’t really register that the pain was there [...] Yeah, that’s what I find a lot with the pains that I get. The more that I am not stimulated, and my mind is not occupied, it is focusing on the pain sensation.”*

Heightened neuropathic pain sensations in the morning, however, may be a result of engagement in certain activities the day prior, in addition to the timing of participation. Participant #1 stated, *“Lower body exercises did increase neuropathic pain in my lower body. Not necessarily directly following, often delayed (12-24 hours delayed).”* Because majority of studies have shown neuropathic pain to be worse as time of day progresses, it is important to note that heightened pain in the morning may not be strictly neuropathic (Swenson & Reeves, 2008). Further research is needed to observe how, and why, neuropathic pain sensations change throughout waking hours in adults with SCI.

7.4 Study Strengths

The following sections outline specific strengths of this study.

7.4.1 Methodology

First, the current study used strict methodology, while aiming to minimize interruption of participants' personal care routines. Second, the ecological aspect of this study allowed measurement to occur within the participants' natural environments. As a result, participants were able to engage in routine behaviours and activities, which enhanced the ecological validity of this study (Shiffman et al., 2007). Although research conducted in a laboratory setting offers the important benefit of experimental control, it is much less clear if the relationships between variables (e.g. exercise, neuropathic pain, affect) observed in the laboratory environment are similar to what occurs in the "real" world (Smyth & Stone, 2003). Third, prior to the start of the study protocol, participants were familiarized with the mEMA and Fitbit technology for a minimum of 1 hour by a trained researcher. This process was designed to mitigate any technological difficulties and ensured complete understanding was reached by each participant.

7.4.2 Protocol

Pilot testing the study protocol was beneficial to determine the response burden involved with the momentary assessments, in addition to the feasibility of the protocol. Measurements occurred 6 times per day over the course of 6 days, similar to the protocol used by Focht and colleagues (2004) with knee osteoarthritis patients. Pilot testing indicated that this schedule was not cumbersome and therefore minimized the probability of reduced data quality (i.e. participants randomly clicking responses; Rolstad et al., 2011). In addition, during daily data collection periods (9AM-9PM), the

researcher provided rapid communication with participants in the event of technological difficulties. This strategy ensured participant prompts were answered in a timely manner, and missing data were kept to a minimum.

7.4.3 Design

This study used a case series design to allow for a deeper understanding of intraindividual differences in neuropathic sensations and affect, both in response to exercise and over the course of each day. Furthermore, using an exploratory, case series design offered the opportunity to simultaneously test and generate hypotheses (Chan & Bhandari, 2011). Although this study had *a priori* hypotheses--which were only partially supported--new knowledge gained from this study allows for the generation of hypotheses that can be tested in future intervention studies. Due to the limited knowledge of how exercise relates to neuropathic pain sensations and affective mood states, a mixed-methods approach was used to gain further insight into participants' subjective experiences of their neuropathic pain and affect, both in response to exercise and over the course of a day. Using both quantitative measures, and structured interviews allowed the researcher to better understand the relationship between exercise, neuropathic pain and affect. Conducting the quantitative and qualitative phases sequentially allowed for participants to expand on their quantitative data (Chow et al., 2009). Thus, by incorporating both types of measurement, a more comprehensive representation of patterns of neuropathic pain, affect, and time of day was captured.

7.5 Study Limitations

Although this study had notable strengths, it also had limitations. These limitations are described in the following sections.

7.5.1 Participants

A small sample of participants was evaluated and therefore this limits generalizability into larger populations. Six participants were included and this sample size was based on the number of cases used in previously published case series in the SCI population (e.g. Bani et al., 2015; Grassner et al., 2015; Jayaraman et al., 2007; Kumru et al., 2016; Pandey et al., 2016; Yozbatiran et al., 2017). A larger sample would have made data analysis difficult due to the large amounts of data collected for each participant. Furthermore, only men were included in the sample, due to the absence of interest expressed by women with SCI. Having a homogenous sample (at least in regards to sex) may potentially be viewed as a strength due to the exploratory nature of this study. However, an exclusively male sample limited the ability to determine if patterns exist between exercise, neuropathic pain and affective mood states experienced by women with SCI. Similarly, recruiting only exercisers as participants made it unclear if patterns also exist between these constructs within non-exercisers with SCI.

7.5.2 mEMA

In regards to technology, utilizing a mobile form of ecological momentary assessment, compared to pen-and-paper questionnaires posed some difficulties for completion of each measure. For example, missing data occurred for some participants as a result of mEMA failing to send prompts for all required intervals in the study period. In addition, some questions were inexplicably excluded in certain surveys received by participants. As a result, some pain composite scores may be slightly inaccurate, specifically if the sensation would have received a greater/lower than average rating by the participant. Complications with technology illustrates the importance of analyzing patterns in neuropathic pain and affect over multiple days, to attempt to mitigate this

limitation. Furthermore, user compliance issues arose with some participants as they had their mobile devices powered off due to previously scheduled events. Lastly, it was difficult to ensure prompts were received/answered immediately following exercise completion. Participants may have exercised for a longer period of time than they had initially stated to the researcher, or not have had immediate access to their mobile devices. Therefore, some neuropathic pain and affective mood states measures may not have been completed within the planned time frame (e.g. 20 minutes) following exercise completion.

7.5.3 Exercise Participation

It may be possible that the 6-day data collection period utilized within this study was not representative of the participant's typical routine. Therefore, including a second measurement period, or extending the study for a longer duration of time may have provided increasingly accurate data regarding typical activities and exercise participation. Furthermore, there was no control over the specific type of exercise being performed by each participant, which could impact neuropathic pain and affective responses. However, the purpose of this study was not to determine "*what*" types of exercise may reduce neuropathic pain or influence overall affect, but rather to determine "*if*" exercise could be used as a potential treatment for reducing neuropathic pain (and simultaneously increase positive affect). Most participants performed aerobic exercise within this study. As a result, it was impossible to determine if the type of exercise (i.e. resistance versus aerobic training) influences neuropathic pain sensations.

Finally, the intensity of exercise was not measured and cannot be determined to be causally related to changes in neuropathic pain and affect. Although participants wore Fitbit Surge watches to capture heart rate data, baseline heart rate measurements were not captured and

therefore only fluctuations and visual peaks could be observed. This lack of baseline data made analysis of the potential effect of exercise intensity on neuropathic pain sensations (Norrbrink et al., 2012), impossible. Future research in this area should include the collection of baseline heart rate data, to allow for evaluation of the effect of exercise intensity on neuropathic pain.

7.5.4 Momentary Assessment

Participants' neuropathic pain sensations may have been exacerbated due to the ecological nature of this study. Increased awareness of the presence of neuropathic pain due to the consistent mEMA prompts may have led to rating neuropathic pain sensations as more severe than usual. However, it was anticipated that heightened neuropathic pain sensations due to increased awareness would remain consistent across the measurement period. Therefore, intraindividual patterns in neuropathic pain were expected to be unchanged, regardless if individual ratings were slightly higher than usual.

Despite these limitations, the reductions in neuropathic pain observed in response to exercise participation at the group level, in addition to reductions in neuropathic pain mirrored by fluctuations in positive affect observed at the individual level are encouraging findings. This preliminary evidence supports the notion that exercise may be a potential treatment option to reduce neuropathic pain, and increase positive affect, in at least some adults with SCI.

8 Conclusion

8.1 Implications and Future Directions

This study provides original contributions to literature examining neuropathic pain and affect in the SCI population in multiple ways: First, to the best of our knowledge, this is the first study to measure neuropathic pain and affect in response to acute exercise in adults with SCI. Secondly, this study presents the first evaluation of the relationship between neuropathic pain and affect in adults with SCI. Third, this is the first study to measure diurnal variations in neuropathic pain and affective states of individuals with SCI. These contributions have implications for researchers, rehabilitation therapists, and adults with SCI.

8.2 Practical Implications

Researchers, rehabilitation therapists, and adults with SCI can all utilize the results from this study. First, with respect to implications for researchers, knowing exercise may reduce neuropathic pain in adults with an SCI, allows researchers to design randomized, controlled trials and further observe neuropathic pain sensations in response to exercise to determine if a causal relationship exists. Intraindividual patterns were observed in this study relative to the changes in neuropathic pain sensations in response to exercise, therefore providing rationale to examine potential variables that may explain these patterns, such as type, intensity, or length of exercise participation. Furthermore, affective mood states can be also evaluated both in response to various types and intensities of exercise, as well as over time. Finally, the utility of using a mobile form of ecological momentary assessment, such as mEMA, to observe diurnal variations in neuropathic pain and affect was demonstrated. In doing so, a methodology was developed for application in future ecological momentary assessment studies in the SCI population.

Second, with respect to applications for rehabilitation therapists, a barrier to physical activity participation often exists for adults with SCI due to the chronic impact of neuropathic pain. As a result, these individuals may avoid, limit, or cease engagement in physical activity and/or rehabilitation (Carpenter et al., 2007; Kim et al., 2011; Scelza et al., 2005). This study provides beneficial information for rehabilitation therapists to assist with exercise promotion in the SCI population. A viable first step in exercise promotion may be for rehabilitation therapists to encourage the use of a momentary assessment tool, such as mEMA. This will allow patients to determine patterns that may exist relative to the presence of their neuropathic pain. As a result, the effectiveness of exercise to potentially reduce neuropathic pain may be maximized.

Based on results from structured exit interviews conducted in this study, rationale is provided for the promotion of momentary assessment of neuropathic pain. Participant #1 reported, *“For certain individuals, it might be useful, especially if engaging in new activities (new exercise pain, new activity, eating differently). I can see it being useful to track neuropathic pain and identify some individual patterns that might arise from new activities, and a good way of targeting what is causing neuropathic pain.”* Furthermore, participant #3 stated, *“It kind of helped me to give me an understanding of my pain[...] I learned that after showering, or working out, or stretching, how it does follow a pattern. Before, I never wrote on a calendar or kept track of it. By doing the assessments, it kind of stored in the back of my head that, well, the last time I scored a different number because I was doing something different. I think it’s a good thing, especially if you track different things over a long time and you can track different patterns.”*

Third, adults with SCI can apply knowledge gained from this study in multiple ways. There is a possibility that active individuals currently avoid exercise participation on days that their neuropathic pain sensations are high. This study may provide rationale for using exercise as

a neuropathic pain reduction technique on these days, and minimize one of the barriers to exercise participation in this population. In addition, exercise may increase feelings of positive affect, which may lead to greater exercise motivation and adherence. This is of importance, because in a 9- month exercise training intervention conducted (Hicks et al., 2003), 50% of participants did not adhere to the entire exercise training intervention. This lack of sustained exercise participation highlights the importance of finding methods to increase exercise adherence for adults with SCI. Finally, the correlation between time of day, neuropathic pain and affect may provide rationale for scheduling activities earlier in the day, as 3 out of 6 participants had greater neuropathic pain throughout the course of the day.

8.3 Conclusion

The results of this project suggest that exercise may be used as either an alternative to, or in conjunction with, pharmacological treatments to acutely reduce neuropathic pain sensations in adults with SCI. Furthermore, exercise may also precede an increase in positive affect within some adults with SCI, as 5 out of 6 participants experienced an increase in positive affect following at least one bout of exercise. Lastly, time of day may play a role in sensations of neuropathic pain or the affective mood state of adults with SCI. Taken together, these findings suggest that exercise may be used to reduce neuropathic pain sensations in adults with SCI, and may simultaneously enhance feelings of pleasure. Thus, engaging in exercise may be a viable recommendation for adults with SCI who suffer from neuropathic pain.

References

- Anson, C. A., & Shepherd, C. (1995). Incidence of secondary complications in spinal cord injury. *International Journal of Rehabilitation Research*, 19(1), 55-66.
- Backonja, M. M., & Stacey, B. (2004). Neuropathic pain symptoms relative to overall pain rating. *The Journal of Pain*, 5(9), 491-497.
- Bani, M. A., Arazpour, M., Farahmand, F., Kashani, R. V., Mousavi, M. E., & Hutchins, S. W. (2015). Comparison of new medial linkage reciprocating gait orthosis and isocentric reciprocating gait orthosis on energy consumption in paraplegic patients: a case series. *Spinal Cord Series and Cases*, 1.
- Barrera-Chacon, J. M., Mendez-Suarez, J. L., Jáuregui-Abrisqueta, M. L., Palazon, R., Barbara-Bataller, E., & García-Obrero, I. (2010). Oxycodone improves pain control and quality of life in anticonvulsant-pretreated spinal cord-injured patients with neuropathic pain. *Spinal Cord*, 49(1), 36-42.
- Bryce, T. N., Biering-Sørensen, F., Finnerup, N. B., Cardenas, D. D., Defrin, R., Lundberg, T., ... & Treede, R. D. (2012). International spinal cord injury pain classification: Part I. Background and description. *Spinal Cord*, 50(6), 413-417.
- Cairns, D. M., Adkins, R. H., & Scott, M. D. (1996). Pain and depression in acute traumatic spinal cord injury: origins of chronic problematic pain? *Archives of physical medicine and rehabilitation*, 77(4), 329-335.
- Cardenas, D. D., Warms, C. A., Turner, J. A., Marshall, H., Brooke, M. M., & Loeser, J. D. (2002). Efficacy of amitriptyline for relief of pain in spinal cord injury: results of a randomized controlled trial. *Pain*, 96(3), 365-373.
- Cardenas, D. D., Nieshoff, E. C., Suda, K., Goto, S. I., Sanin, L., Kaneko, T., ... & Whalen, E. (2013). A randomized trial of pregabalin in patients with neuropathic pain due to spinal cord injury. *Neurology*, 80(6), 533-539.
- Carey, T. S., & Boden, S. D. (2003). A critical guide to case series reports. *Spine*, 28(15), 1631-1634.
- Carpenter, C., Forwell, S. J., Jongbloed, L. E., & Backman, C. L. (2007). Community participation after spinal cord injury. *Archives of physical medicine and rehabilitation*, 88(4), 427-433.
- Chan, K., & Bhandari, M. (2011). Three-minute critical appraisal of a case series article. *Indian journal of orthopaedics*, 45(2), 103.

Chow, M. Y. K., Quine, S., & Li, M. (2010). The benefits of using a mixed methods approach—quantitative with qualitative—to identify client satisfaction and unmet needs in an HIV healthcare centre. *AIDS care*, 22(4), 491-498.

Davies, A. L., Hayes, K. C., & Dekaban, G. A. (2007). Clinical correlates of elevated serum concentrations of cytokines and autoantibodies in patients with spinal cord injury. *Archives of physical medicine and rehabilitation*, 88(11), 1384-1393.

Detloff, M. R., Smith, E. J., Molina, D. Q., Ganzer, P. D., & Houlié, J. D. (2014). Acute exercise prevents the development of neuropathic pain and the sprouting of non-peptidergic (GDNF-and artemin-responsive) c-fibers after spinal cord injury. *Experimental neurology*, 255, 38-48.

Devillard, X., Rimaud, D., Roche, F., & Calmels, P. (2007). Effects of training programs for spinal cord injury. In *Annales de réadaptation et de médecine physique*, 50(6), 490-498.

Dijkers, M., Bryce, T., Zanca, J. (2009). Prevalence of chronic pain after traumatic spinal cord injury: a systematic review. *Journal of rehabilitation research and development*, 46(1), 13.

Ditor, D. S., Kamath, M. V., MacDonald, M. J., Bugaresti, J., McCartney, N., & Hicks, A. L. (2005). Effects of body weight-supported treadmill training on heart rate variability and blood pressure variability in individuals with spinal cord injury. *Journal of Applied Physiology*, 98(4), 1519-1525.

Dua, J. K. (1993). The role of negative affect and positive affect in stress, depression, self-esteem, assertiveness, Type A behaviors, psychological health, and physical health. *Genetic, Social, and General Psychology Monographs*.

Ekkekakis, P. (2013). *The measurement of affect, mood, and emotion: A guide for health-behavioral research*. Cambridge University Press.

Farrar, J. T., Young, J. P., LaMoreaux, L., Werth, J. L., & Poole, R. M. (2001). Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*, 94(2), 149-158.

Finnerup, N. B. (2013). Pain in patients with spinal cord injury. *Pain*, 154, S71-S76.

Finnerup, N. B., & Bastrup, C. (2012). Spinal cord injury pain: mechanisms and management. *Current pain and headache reports*, 16(3), 207-216.

Focht, B. C., Ewing, V., Gauvin, L., & Rejeski, W. J. (2002). The unique and transient impact of acute exercise on pain perception in older, overweight, or obese adults with knee osteoarthritis. *Annals of Behavioral Medicine*, 24(3), 201-210.

Focht, B. C., Gauvin, L., & Rejeski, W. J. (2004). The contribution of daily experiences and acute exercise to fluctuations in daily feeling states among older, obese adults with knee osteoarthritis. *Journal of Behavioral Medicine*, 27(2), 101-121.

- Ford E.S. (2002). Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. adults. *Epidemiology*, 13(5), 561–568.
- Galer, B. S., & Jensen, M. P. (1997). Development and preliminary validation of a pain measure specific to neuropathic pain The Neuropathic Pain Scale. *Neurology*, 48(2), 332-338.
- Gauvin, L., & Rejeski, W. J. (1993). The exercise-induced feeling inventory: Development and initial validation. *Journal of Sport and Exercise Psychology*, 15(4), 403-423.
- Gilboa-Schechtman, E., & Foa, E.B. (2001). Patterns of recovery from trauma: The use of intraindividual analysis. *Journal of Abnormal Psychology*, 110(3), 392.
- Gilron, I., Bailey, J. M., & Vandenkerkhof, E. G. (2013). Chronobiological characteristics of neuropathic pain: clinical predictors of diurnal pain rhythmicity. *The Clinical journal of pain*, 29(9), 755-759.
- Grassner, L., Geuther, M., Mach, O., Bühren, V., Vastmans, J., & Maier, D. (2015). Charcot spinal arthropathy: an increasing long-term sequel after spinal cord injury with no straightforward management. *Spinal Cord Series and Cases*, 1.
- Grigorean, V. T., Sandu, A. M., Popescu, M., Iacobini, M. A., Stoian, R., Neascu, C., & Popa, F. (2009). Cardiac dysfunctions following spinal cord injury. *Journal of medicine and life*, 2(2), 133.
- Hagen, E. M. (2015). Acute complications of spinal cord injuries. *World journal of orthopedics*, 6(1), 17.
- Hagen, E. M., & Rekand, T. (2015). Management of Neuropathic Pain Associated with Spinal Cord Injury. *Pain and Therapy*, 4(1), 51–65.
- Hagglund, K. J., Haley, W. E., Reveille, J. D., & Alarcon, G. S. (1989). Predicting individual differences in pain and functional impairment among patients with rheumatoid arthritis. *Arthritis Rheum*, 32(7), 851-858.
- Hardy, C. J., & Rejeski, W. J. (1989). Not what, but how one feels: The measurement of affect during exercise. *Journal of Sport and Exercise Psychology*, 11(3), 304-317.
- Henwood, P., Ellis, J., Logan, J., Dubouloz, C. J., & D'eon, J. (2012). Acceptance of chronic neuropathic pain in spinal cord injured persons: a qualitative approach. *Pain management nursing*, 13(4), 215-222.
- Hicks, A. L., Martin, K. A., Ditor, D. S., Latimer, A. E., Craven, C., Bugaresti, J., & McCartney, N. (2003). Long-term exercise training in persons with spinal cord injury: effects on strength, arm ergometry performance and psychological well-being. *Spinal cord*, 41(1), 34-43.

Hoffman, M. D., Shepanski, M. A., Ruble, S. B., Valic, Z., Buckwalter, J. B., & Clifford, P. S. (2004). Intensity and duration threshold for aerobic exercise-induced analgesia to pressure pain. *Archives of physical medicine and rehabilitation*, 85(7), 1183-1187.

Hutchinson, K. J., Gómez-Pinilla, F., Crowe, M. J., Ying, Z., & Basso, D. M. (2004). Three exercise paradigms differentially improve sensory recovery after spinal cord contusion in rats. *Brain*, 127(6), 1403-1414.

IASP. ISAP taxonomy. 2012; Available at: <http://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698&navItemNumber=576>.

Jacobs P.L. & Nash, M.S. (2004). Exercise recommendations for individuals with spinal cord injury. *Sports Med*, 34, 727-751.

Janssen, S. A. (2002). Negative affect and sensitization to pain. *Scandinavian journal of psychology*, 43(2), 131-137.

Jayaraman, A., Shah, P., Gregory, C., Bowden, M., Stevens, J., Bishop, M., ... Vandeborne, K. (2008). Locomotor Training and Muscle Function After Incomplete Spinal Cord Injury: Case Series. *The Journal of Spinal Cord Medicine*, 31(2), 185–193.

Jensen, M. P., Chodroff, M. J., & Dworkin, R. H. (2007). The impact of neuropathic pain on health-related quality of life Review and implications. *Neurology*, 68(15), 1178-1182.

Jensen, T. S., & Finnerup, N. B. (2014). Allodynia and hyperalgesia in neuropathic pain: clinical manifestations and mechanisms. *The Lancet Neurology*, 13(9), 924-935.

Kehn, M., & Kroll, T. (2009). Staying physically active after spinal cord injury: a qualitative exploration of barriers and facilitators to exercise participation. *BMC Public Health*, 9, 168.

Kim, I. T., Mun, J. H., Jun, P. S., Kim, G. C., Sim, Y.-J., & Jeong, H. J. (2011). Leisure Time Physical Activity of People with Spinal Cord Injury: Mainly with Clubs of Spinal Cord Injury Patients in Busan-Kyeongnam, Korea. *Annals of Rehabilitation Medicine*, 35(5), 613–626. <http://doi.org/10.5535/arm.2011.35.5.613>

Kratz, A. L., Ehde, D. M., Bombardier, C. H., Kalpakjian, C. Z., & Hanks, R. A. (2017). Pain acceptance decouples the momentary associations between pain, pain interference, and physical activity in the daily lives of people with chronic pain and spinal cord injury. *The Journal of Pain*, 18(3), 319-331.

Kukkar, A., Bali, A., Singh, N., & Jaggi, A. S. (2013). Implications and mechanism of action of gabapentin in neuropathic pain. *Archives of pharmacological research*, 36(3), 237-251.

Kumru, H., Albu, S., Vidal, J., Barrio, M., & Santamaria, J. (2016). Dopaminergic treatment of restless legs syndrome in spinal cord injury patients with neuropathic pain. *Spinal Cord Series*

and Cases, 2.

Lee, S., Zhao, X., Hatch, M., Chun, S., & Chang, E. (2013). Central Neuropathic Pain in Spinal Cord Injury. *Critical Reviews in Physical and Rehabilitation Medicine*, 25(3-4), 159–172.

Martin Ginis, K. A., Latimer, A. E., Hicks, A. L., & Craven, B. C. (2005). Development and evaluation of an activity measure for people with spinal cord injury. *Medicine and science in sports and exercise*, 37(7), 1099-1111.

Martin Ginis, K. A., & Latimer, A. E. (2007). The effects of single bouts of body-weight supported treadmill training on the feeling states of people with spinal cord injury. *Spinal Cord*, 45(1), 112-115.

Martin Ginis, K. A., Jörgensen, S., & Stapleton, J. (2012). Exercise and sport for persons with spinal cord injury. *Archives of physical medicine and rehabilitation*, 4(11), 894-900.

Maynard, F. M., Bracken, M. B., Creasey, G. J. F. D., Ditunno, J. F., Donovan, W. H., Ducker, T. B., ... & Waters, R. L. (1997). International standards for neurological and functional classification of spinal cord injury. *Spinal cord*, 35(5), 266-274.

Moskowitz, D. S., & Young, S. N. (2006). Ecological momentary assessment: what it is and why it is a method of the future in clinical psychopharmacology. *Journal of psychiatry & neuroscience*, 31(1), 13.

Moulin, D. E., Clark, A. J., Gilron, I., Ware, M. A., Watson, C. P. N., Sessle, B. J., ... & Peng, P. (2007). Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. *Pain Research and Management*, 12(1), 13-21.

Nas, K., Yazmalar, L., Şah, V., Aydın, A., & Öneş, K. (2015). Rehabilitation of spinal cord injuries. *World journal of orthopedics*, 6(1), 8.

Nepomuceno, C., Fine, P. R., Richards, J. S., Gowens, H., Stover, S. L., Rantanuabol, U., & Houston, R. (1979). Pain in patients with spinal cord injury. *Archives of physical medicine and rehabilitation*, 60(12), 605-609.

Norrbrink, C., & Lundeberg, T. (2009). Tramadol in neuropathic pain after spinal cord injury: a randomized, double-blind, placebo-controlled trial. *The Clinical journal of pain*, 25(3), 177-184.

Norrbrink C, Lundeberg T, Wahman K, Bjerkefors A. (2012). Effects of an exercise programme on musculoskeletal and neuropathic pain after spinal cord injury—Results from a seated double-poling ergometer study. *Spinal Cord*, 50(6), 457–461.

Odrich, M., Bailey, J. M., Cahill, C. M., & Gilron, I. (2006). Chronobiological characteristics of painful diabetic neuropathy and postherpetic neuralgia: diurnal pain variation and effects of analgesic therapy. *Pain*, 120(1), 207-212.

- Padawer, W. J., & Levine, F. M. (1992). Exercise-induced analgesia: fact or artifact?. *Pain*, 48(2), 131-135.
- Pandey, S., Holla, V. V., Rizvi, I., Qavi, A., & Shukla, R. (2016). Can vitamin B12 deficiency manifest with acute posterolateral or posterior cord syndrome?. *Spinal Cord Series and Cases*, 2.
- Pedersen, B. K., & Febbraio, M. A. (2008). Muscle as an endocrine organ: focus on muscle-derived interleukin-6. *Physiological reviews*, 88(4), 1379-1406.
- Petersen, A. M. W., & Pedersen, B. K. (2005). The anti-inflammatory effect of exercise. *Journal of applied physiology*, 98(4), 1154-1162.
- Phillips, D. L., & Clancy, K. J. (1972). Some effects of "social desirability" in survey studies. *American Journal of Sociology*, 77(5), 921-940.
- Prince, S. A., Adamo, K. B., Hamel, M. E., Hardt, J., Gorber, S. C., & Tremblay, M. (2008). A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, 5(1), 56.
- Ragnarsson, K. (1997). Management of pain in persons with spinal cord injury. *The journal of spinal cord medicine*, 20(2), 187-199.
- Rejeski, W. J., Ettinger Jr, W. H., Shumaker, S., Heuser, M. D., James, P., Monu, J., & Burns, R. (1995). The evaluation of pain in patients with knee osteoarthritis: the knee pain scale. *The Journal of rheumatology*, 22(6), 1124-1129.
- Rintala, D. H., Holmes, S. A., Courtade, D., Fiess, R. N., Tastard, V., & Loubser, P. G. (2007). Comparison of the Effectiveness of Amitriptyline and Gabapentin on Chronic Neuropathic Pain in Persons With Spinal Cord Injury. *Archives of Physical Medicine and Rehabilitation*, 88, 1547-1560.
- Rodrigues, D., Tran, Y., Wijesuriya, N., Guest, R., Middleton, J., & Craig, A. (2013). Pain Intensity and Its Association with Negative Mood States in Patients with Spinal Cord Injury. *Pain and Therapy*, 2(2), 113-119.
- Rolstad, S., Adler, J., & Rydén, A. (2011). Response burden and questionnaire length: is shorter better? A review and meta-analysis. *Value in Health*, 14(8), 1101-1108.
- Scelza, W. M., Kalpakjian, C. Z., Zemper, E. D., & Tate, D. G. (2005). Perceived barriers to exercise in people with spinal cord injury. *American Journal of Physical Medicine & Rehabilitation*, 84(8), 576-583.
- Shiffman, S., Stone, A. A., & Hufford, M. R. (2008). Ecological momentary assessment. *Annual Review of Clinical Psychology*, 4, 1-32.
- Siddall, P. J., Taylor, D. A., McClelland, J. M., Rutkowski, S. B., & Cousins, M. J. (1999). Pain

report and the relationship of pain to physical factors in the first 6 months following spinal cord injury. *Pain*, 81(1), 187-197.

Siddall, P. J., & Loeser, J. D. (2001). Pain following spinal cord injury. *Spinal cord*, 39(2), 63.

Siddall, P. J., McClelland, J. M., Rutkowski, S. B., & Cousins, M. J. (2003). A longitudinal study of the prevalence and characteristics of pain in the first 5 years following spinal cord injury. *Pain*, 103(3), 249-257.

Stevens, S. L., Caputo, J. L., Fuller, D. K., & Morgan, D. W. (2008). Physical activity and quality of life in adults with spinal cord injury. *The journal of spinal cord medicine*, 31(4), 373-378.

da Silva Alves, E., de Aquino Lemos, V., Ruiz da Silva, F., Lira, F. S., dos Santos, R. V. T., Rosa, J. P. P., ... & de Mello, M. T. (2013). Low-grade inflammation and spinal cord injury: exercise as therapy? *Mediators of inflammation*.

Smedstad, L. M., Mourn, T., Vaglum, P., & Kvien, T. K. (1996). The impact of early rheumatoid arthritis on psychological distress. *Scandinavian journal of rheumatology*, 25(6), 377-382.

Smyth, J. M., & Stone, A. A. (2003). Ecological momentary assessment research in behavioral medicine. *Journal of Happiness studies*, 4(1), 35-52.

Stagg, N. J., Mata, H. P., Ibrahim, M. M., Henriksen, E. J., Porreca, F., Vanderah, T. W., & Malan, T. P. (2011). Regular exercise reverses sensory hypersensitivity in a rat neuropathic pain model role of endogenous opioids. *Anesthesiology: The Journal of the American Society of Anesthesiologists*, 114(4), 940-948.

Steensberg, A., Hall, G., Osada, T., Sacchetti, M., Saltin, B., & Pedersen, B. K. (2000). Production of interleukin-6 in contracting human skeletal muscles can account for the exercise-induced increase in plasma interleukin-6. *The Journal of physiology*, 529(1), 237-242.

Strian, F., Lautenbacher, S., Galfe, G., & Hölzl, R. (1989). Diurnal variations in pain perception and thermal sensitivity. *Pain*, 36(1), 125-131.

Svebak, S., & Murgatroyd, S. (1985). Metamotivational dominance: A multimethod validation of reversal theory constructs. *Journal of Personality and Social Psychology*, 48(1), 107.

Thiele, C., Laireiter, A. R., & Baumann, U. (2002). Diaries in clinical psychology and psychotherapy: A selective review. *Clinical Psychology & Psychotherapy*, 9(1), 1-37.

Tsang, K. L., Yong, H., J. R., & Ding, D. (2016). Measuring Heart Rate In Manual Wheelchair Users During Exercise And Free-Living Activity With The Latest Fitbit Surge Monitor. *Conference: Rehabilitation Engineering and Assistive Technology Society of North America*.

Tuomenoksa, M. (2013). ilumivu: Ecological momentary assessment. *Available:*

<http://www.ilumivu.com/index.php?section=41&chapter=54>.

Uçeyler N, Eberle T, Rolke R, Birklein F, Sommer C. (2007). Differential expression patterns of cytokines in complex regional pain syndrome. *Pain*, 132, 195–205.

Warms, C. A., Turner, J. A., Marshall, H. M., & Cardenas, D. D. (2002). Treatments for chronic pain associated with spinal cord injuries: many are tried, few are helpful. *The Clinical journal of pain*, 18(3), 154-163.

Watson, D., & Clark, L. A. (1997). Measurement and mismeasurement of mood: Recurrent and emergent issues. *Journal of personality assessment*, 68(2), 267-296.

World Health Organization Fact Sheet. 2013; Available at:
<http://www.who.int/mediacentre/factsheets/fs384/en/>

Yozbatiran, N., Keser, Z., Hasan, K., Stampas, A., Korupolu, R., Kim, S., ... & Francisco, G. E. (2017). White matter changes in corticospinal tract associated with improvement in arm and hand functions in incomplete cervical spinal cord injury: pilot case series. *Spinal Cord Series and Cases*, 3, scsandc201728.

APPENDICES

Appendix A: Study Materials

Consent Form

Sociodemographic Questionnaire

Neuropathic Pain Scale

Feeling Scale

Felt Arousal Scale

Qualitative Structured Interview



Consent to Participate in Smartphone-based Survey Research

“Do patterns exist between exercise, neuropathic pain and affect in individuals with paraplegia?”

Identification of Investigator and Purpose of Study

You are invited to participate in a research study, entitled “Do patterns exist between exercise, neuropathic pain and affect in individuals with paraplegia.” This study is being conducted by student investigator Kendra Todd of the University of British Columbia, for partial fulfillment of the Degree Master of Science. She may be reached at (519)-546-3496 and/or ktodd03@mail.ubc.ca. Dr. Kathleen Martin Ginis is the Principal Investigator of this study. She can be reached at 250-807-9768 and/or Kathleen_martin.ginis@ubc.ca. Kendra Todd is a Master’s of Science Candidate in the School of Health and Exercise Sciences and currently holds a Bachelor of Science (Honours) degree. Dr. Kathleen Martin Ginis is a Professor in the School of Health and Exercise Sciences and a Principal Investigator at ICORD (International Collaboration on Repair Discoveries).

The purpose of this research study is to observe neuropathic pain (NP) experienced by paraplegics on days with and without exercise and determine if patterns exist. A secondary purpose of this study is to determine if there are associations between mood and neuropathic pain on days with and without exercise. Your participation in the study will contribute to a better understanding of how individuals with paraplegia experience NP symptoms, and how these symptoms vary as a result of exercise participation. You are free to contact the student and Principal Investigator at the above address and phone number to discuss the study. You must be at least 18 years old to participate.

If you agree to participate:

- The free Smartphone Application “mEMA” will send the Neuropathic Pain Scale questionnaire, Felt Arousal Scale, and Feeling State Measure. These questionnaires will evaluate your symptoms of NP and your current mood at the time of signal receipt. Completion of these measures will take approximately 35-60 minutes per day, spread out over a 12-hour period. On Day #4 and Day #7 of the study protocol, you will be asked to complete an interview about physical activity participation which will take approximately 20-30 minutes. This research protocol will occur over 6 consecutive days.
- The research team will provide participants with a copy of their individual data, in addition to a summary of aggregate data
- **You will be compensated up to \$150.00. (\$25.00/day of full completion)**

Risks/Benefits/Confidentiality of Data

There are some possible risks such as exacerbation of pain due to continuous reminders of its presence, however every effort has been made to minimize this potential risk. Questionnaires will only be sent 6x/day to capture the essence of momentary data, while reducing the risk of consistent pain reminders. There will be no costs for participating, however minimal cell phone data charges may ensue. This online survey company is hosted by a web survey company located in the USA and as such is subject to U.S. laws, in particular, the US Patriot Act which allows authorities access to the records of internet service providers, if necessary. If you choose to participate in the survey, you understand that your responses to

the survey questions will be stored in the USA, and the researchers conducting this study will access your data from the USA. The security and privacy policy for the web survey company can be found at the following link: <https://ilumivu.com/solutions/ecological-momentary-assessment-app/secure-and-compliant/>. No personally identifying information will be included in the questionnaires, and mEMA identification will be through a unique code. All data collected from mEMA will be encrypted prior to being sent to the cloud-based storage database, which has no unauthorized data access. Your name, email address and telephone number will be kept by the research team during the data collection phase for tracking purposes only. Only the researchers named on this project will have access to your data. Personally identifying information will be removed from the final dataset. Thesis documents are published online on cIRcle, therefore results from this project will be publically available on the internet. Internal funding from the University of British Columbia on behalf of Dr. Kathleen Martin Ginis will sponsor this study.

Participation or Withdrawal

Your participation in this study is voluntary. You may decline to answer any question and you have the right to withdraw from participation at any time. You will be asked to complete a demographic questionnaire. You will be provided with a Fitbit Surge, be required to download the Smartphone application “mEMA” and will receive training how to utilize these forms of technology. If you live within a 30km radius of the University of British Columbia Okanagan campus, training will occur on campus. If you live outside of these geographical limits, or if you are unable to attend Campus, training will occur on Skype or over the phone. Fitbit Surges are required to be returned to the principal investigator through prepaid postage. Withdrawal will not affect your relationship with the University of British Columbia in anyway. If you do not want to participate either simply stop participating or delete the Smartphone application. If you choose to withdraw from this study your completed data may still be analyzed.

If you do not want to receive any more reminders, you may contact the research team at ktodd03@mail.ubc.ca or (519)-546-3496.

Contacts

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the UBC Office of Research Ethics at 604-822-8598 or if long distance e-mail RSIL@ors.ubc.ca or call toll free 1-877-822-8598.

By replying to this email stating “I (your name) consent to participate in this research study”, you are consenting to participate in this research. You have two days to respond to this email, beginning the date of email receipt.

Please print a copy of this document for your records.

Sociodemographic Questionnaire

Demographic Information

Age: _____

Sex: [M] [F]

Date of SCI: _____

Level of SCI: _____

Cause: _____

Completeness of Injury:

(A) Complete ☐

(B) Incomplete ☐

(C) Don't Know ☐

What is your primary mode of mobility outside your home?

Manual Wheelchair ☐

Power Wheelchair ☐

Walker ☐

Braces ☐

Cane ☐

Walk Independently ☐

Which of the following describes your ethnicity?

☐ White ☐ Native Canadian ☐ Black ☐ Asian Other: _____

What is the highest level of education you have completed?

☐ High School ☐ College ☐ University ☐ Post Graduate Other: _____

What is your marital status?

☐ Single ☐ Common Law ☐ Married ☐ Divorced ☐ Widowed

How long have you been diagnosed with Neuropathic Pain? _____

Feeling Scale

Feeling Scale (FS) (Hardy & Rejeski, 1989)

While participating in exercise, it is common to experience changes in mood. Some individuals find exercise pleasurable, whereas others find it to be unpleasant. Additionally, feeling may fluctuate across time. That is, one might feel good and bad a number of times during exercise. Scientists have developed this scale to measure such responses.

+5 Very good

+4

+3 Good

+2

+1 Fairly good

0 Neutral

-1 Fairly bad

-2

-3 Bad

-4

-5 Very bad

Felt Arousal Scale

FELT AROUSAL SCALE (FAS)

(Svebak & Murgatroyd, 1985)

Estimate here how aroused you actually feel. Do this by circling the appropriate number. By “arousal” we meant how “worked-up” you feel. You might experience high arousal in one of a variety of ways, for example as excitement or anxiety or anger. Low arousal might also be experienced by you in one of a number of different ways, for example as relaxation or boredom or calmness.

1 LOW AROUSAL

2

3

4

5

6 HIGH AROUSAL

Neuropathic Pain Scale

1. Please use the scale below to tell us how intense your pain is. Place an "X" through the number that best describes the intensity of your pain.													
No pain	0	1	2	3	4	5	6	7	8	9	10	The most intense pain sensation imaginable	
2. Please use the scale below to tell us how sharp your pain feels. Words used to describe "sharp" feelings include "like a knife," "like a spike," "jabbing" or "like jolts."													
Not sharp	0	1	2	3	4	5	6	7	8	9	10	The most sharp sensation imaginable ("like a knife")	
3. Please use the scale below to tell us how hot your pain feels. Words used to describe very hot pain include "burning" and "on fire."													
Not hot	0	1	2	3	4	5	6	7	8	9	10	The most hot sensation imaginable ("on fire")	
4. Please use the scale below to tell us how dull your pain feels. Words used to describe very dull pain include "like a dull toothache," "dull pain," "aching" and "like a bruise."													
Not dull	0	1	2	3	4	5	6	7	8	9	10	The most dull sensation imaginable	
5. Please use the scale below to tell us how cold your pain feels. Words used to describe very cold pain include "like ice" and "freezing."													
Not cold	0	1	2	3	4	5	6	7	8	9	10	The most cold sensation imaginable ("freezing")	
6. Please use the scale below to tell us how sensitive your skin is to light touch or clothing. Words used to describe sensitive skin include "like sunburned skin" and "raw skin."													
Not sensitive	0	1	2	3	4	5	6	7	8	9	10	The most sensitive sensation imaginable ("raw skin")	
7. Please use the scale below to tell us how itchy your pain feels. Words used to describe itchy pain include "like poison oak" and "like a mosquito bite."													
Not itchy	0	1	2	3	4	5	6	7	8	9	10	The most itchy sensation imaginable ("like poison oak")	

9. Now that you have told us the different physical aspects of your pain, the different types of sensations, we want you to tell us overall how **unpleasant** your pain is to you. Words used to describe very unpleasant pain include "miserable" and "intolerable." Remember, pain can have a low intensity, but still feel extremely unpleasant, and some kinds of pain can have a high intensity but be very tolerable. With this scale, please tell us how **unpleasant** your pain feels.

Not unpleasant

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 The most unpleasant sensation imaginable ("intolerable")

10. Lastly, we want you to give us an estimate of the severity of your deep versus surface pain. We want you to rate each location of pain separately. We realize that it can be difficult to make these estimates, and most likely it will be a "best guess," but please give us your best estimate.

HOW INTENSE IS YOUR *DEEP* PAIN?

No deep pain

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

The most intense deep pain sensation imaginable

HOW INTENSE IS YOUR *SURFACE* PAIN?

No surface pain

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

The most intense surface pain sensation imaginable

Qualitative Structured Exit Interview

- 1) Can you tell me about any fluctuations you may have noticed in your neuropathic pain since the beginning of this study?
- 2) Please tell me about your experiences with using mEMA to capture information about your neuropathic pain and mood?
- 3) Were the last 6 days a true representation of your typical weekly routine?
- 4) Do you think mEMA is a useful way for helping people learn about and/or manage neuropathic pain?

Appendix B: Bivariate Pearson's Correlation Coefficient Analyses (NP, Feeling Scale, Felt Arousal)

Participant 1

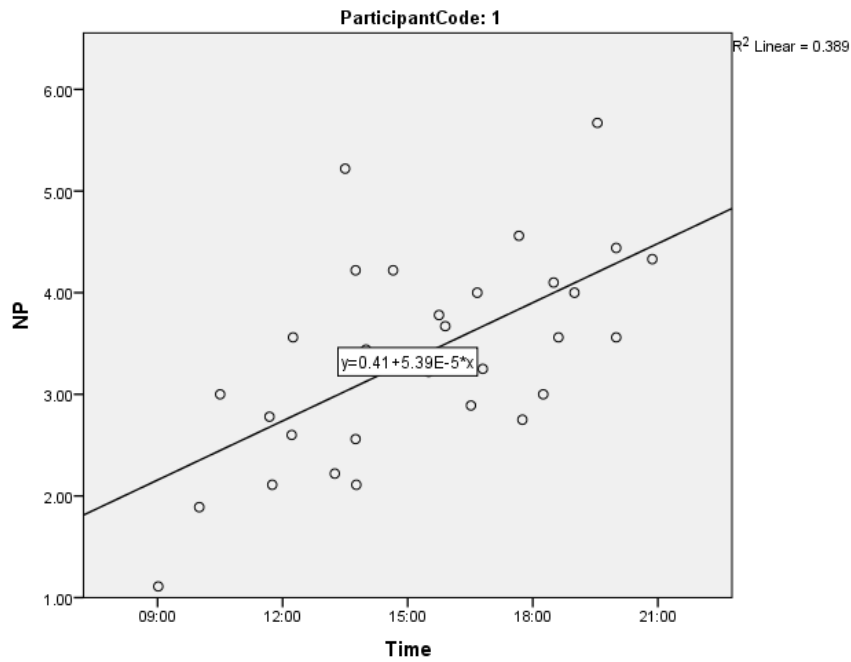


Figure 7: Scatterplot of Bivariate Pearson's Correlation Coefficient for NP and Time

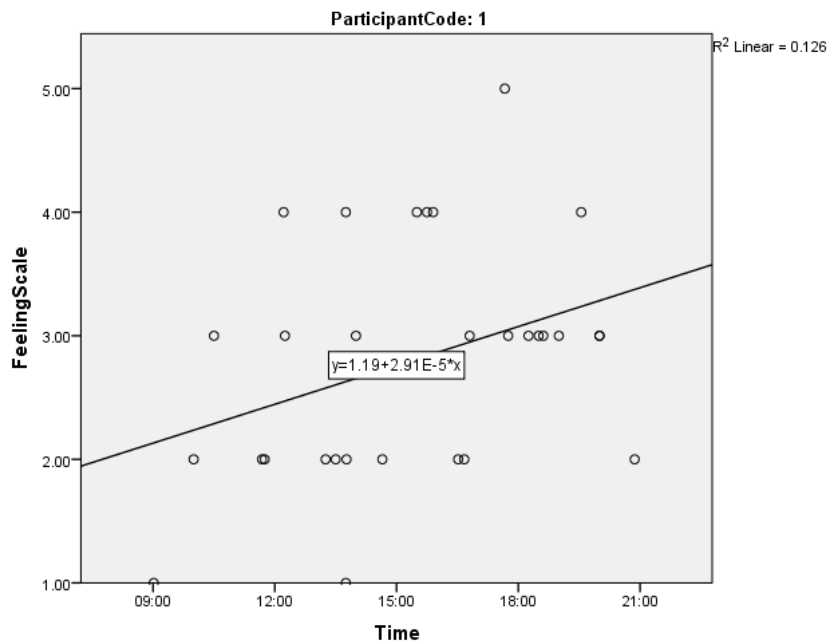


Figure 8: Scatterplot of Bivariate Pearson's Correlation Coefficient for Feeling Scale and Time

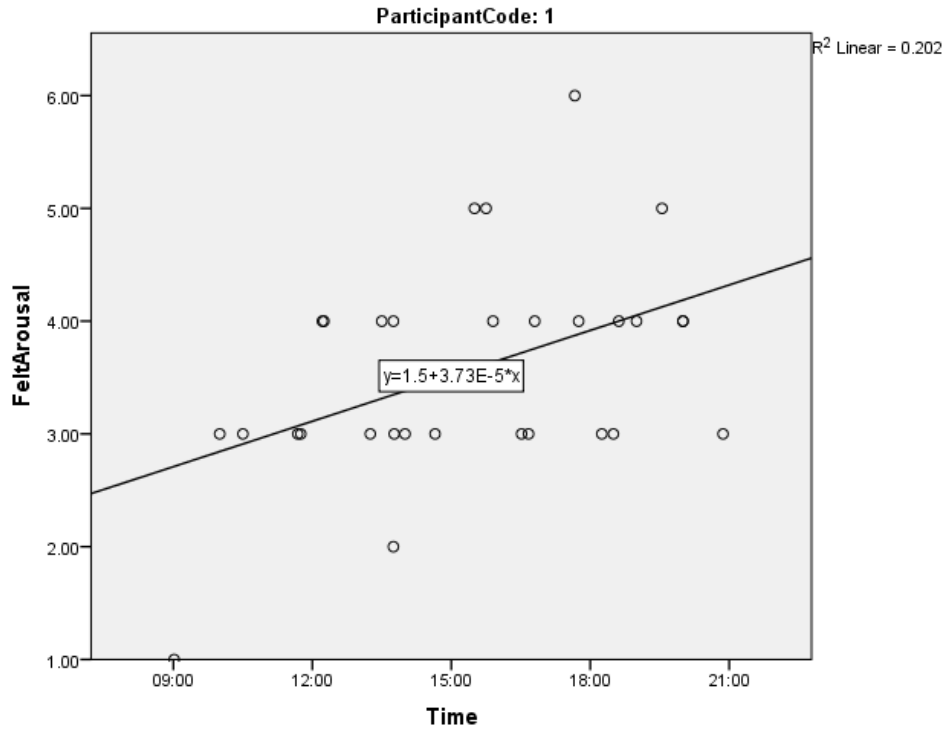


Figure 9: Scatterplot of Bivariate Pearson's Correlation Coefficient for Felt Arousal and Time

Participant 2

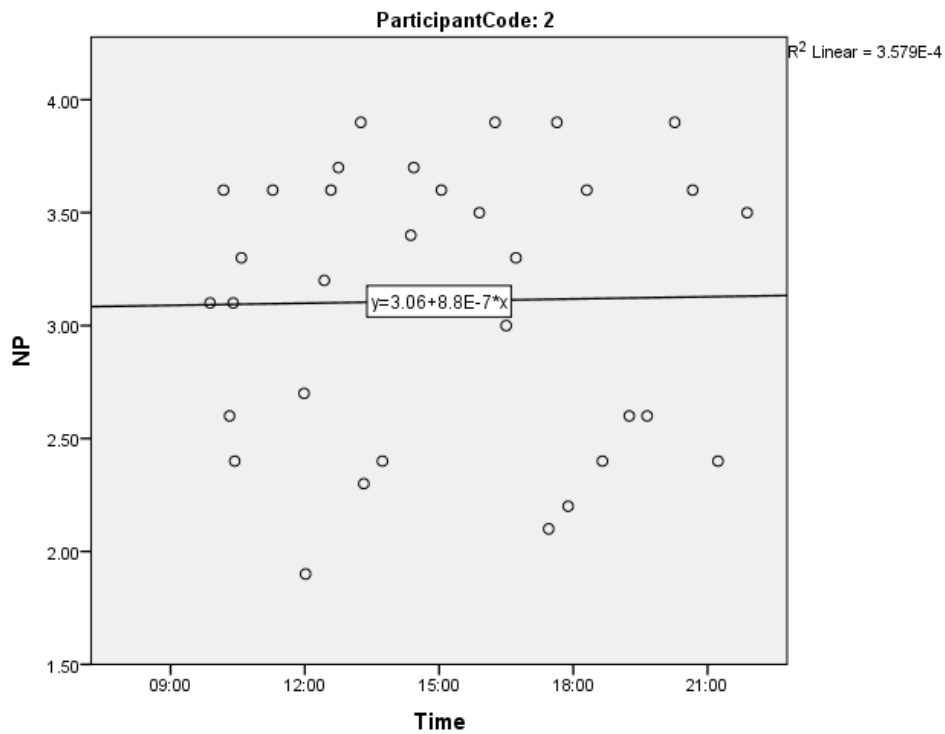


Figure 10: Scatterplot of Bivariate Pearson's Correlation Coefficient for NP and Time



Participant 3

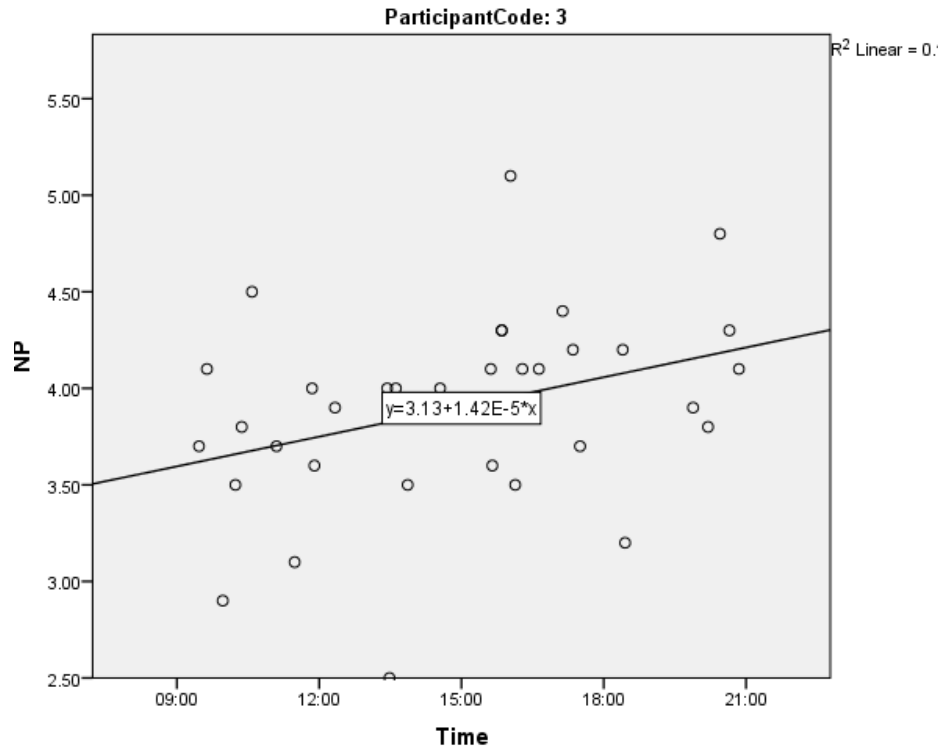


Figure 13: Scatterplot of Bivariate Pearson's Correlation Coefficient for NP and Time

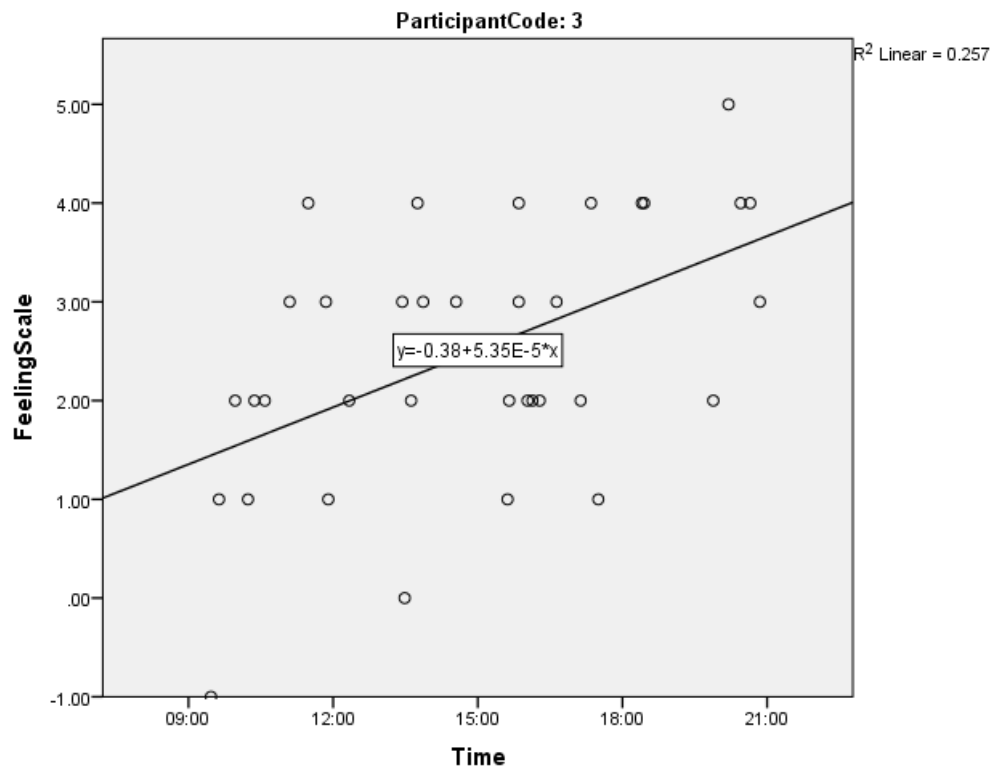


Figure 14: Scatterplot of Bivariate Pearson's Correlation Coefficient for Feeling Scale and Time

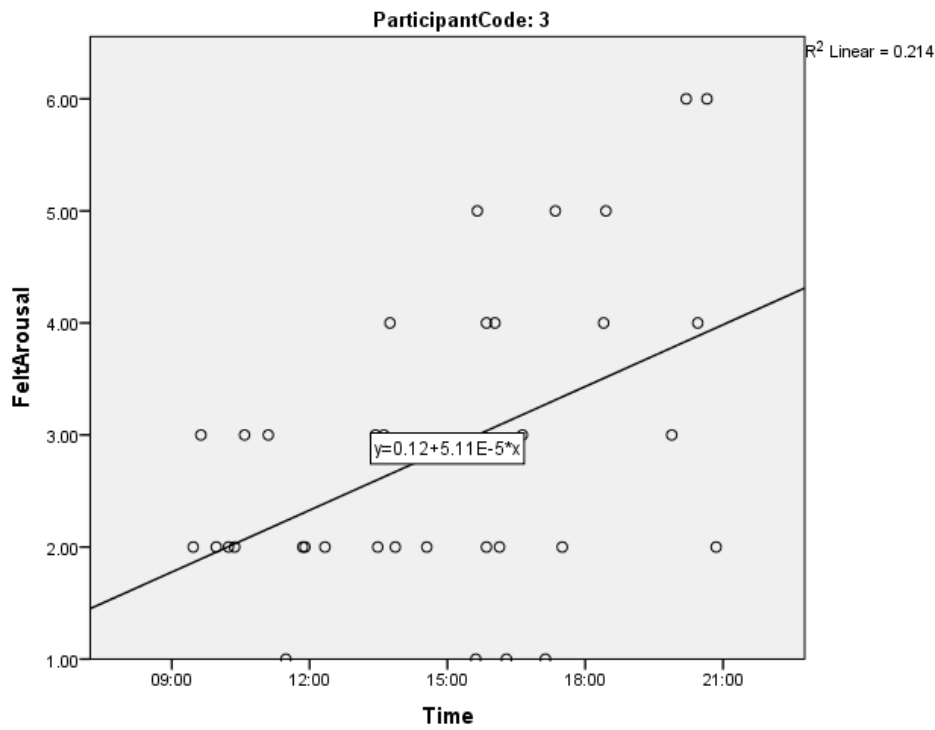


Figure 15: Scatterplot of Bivariate Pearson's Correlation Coefficient for Felt Arousal and Time

Participant 4

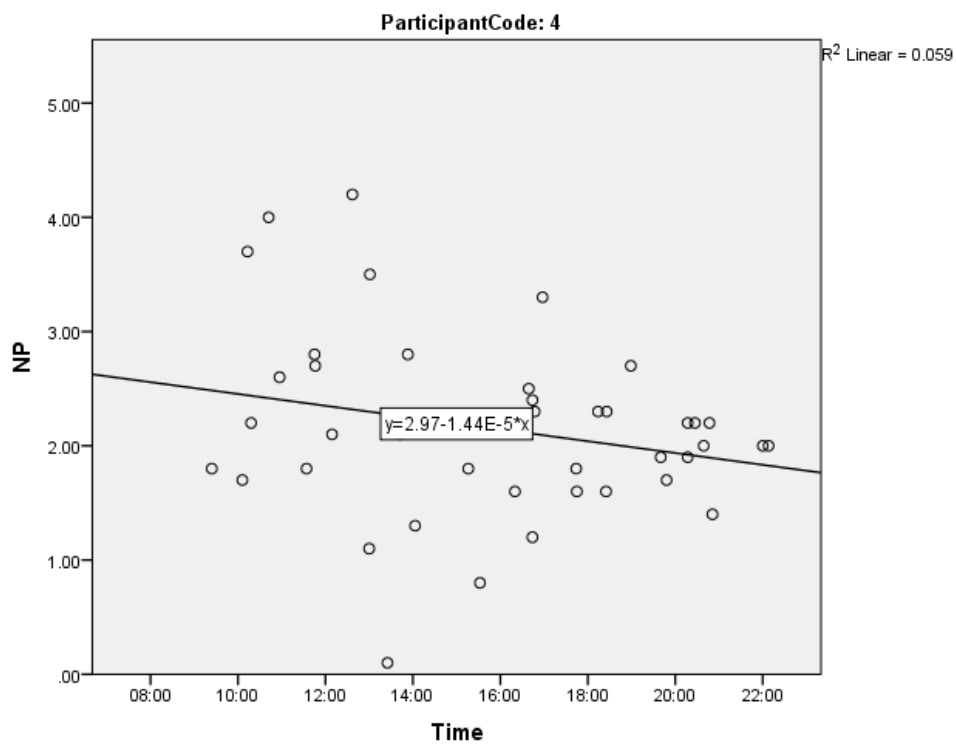


Figure 16: Scatterplot of Bivariate Pearson's Correlation Coefficient for NP and Time

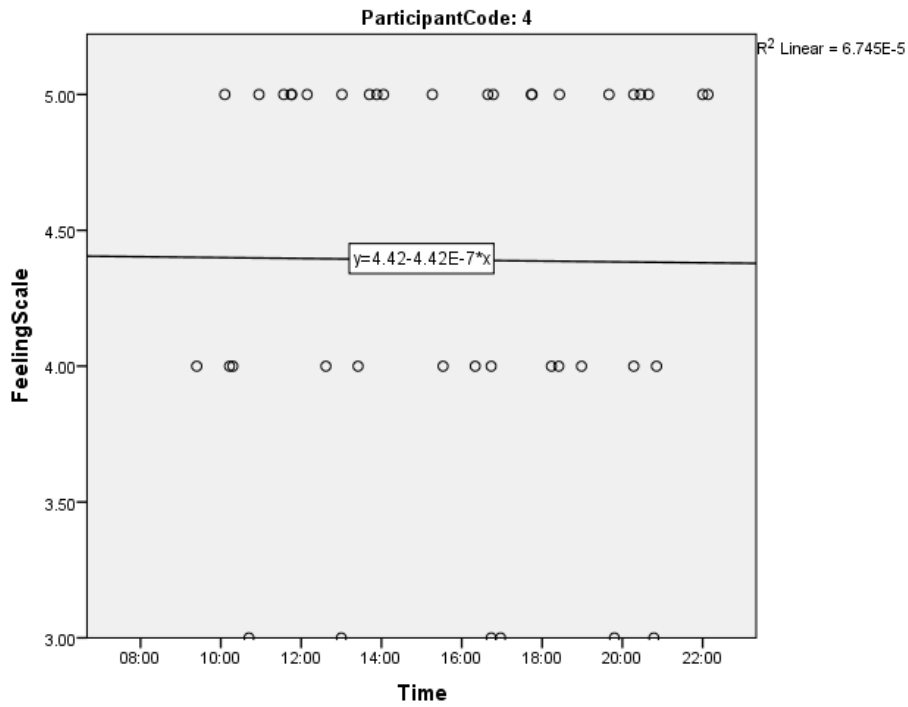


Figure 17: Scatterplot of Bivariate Pearson's Correlation Coefficient for Feeling Scale and Time

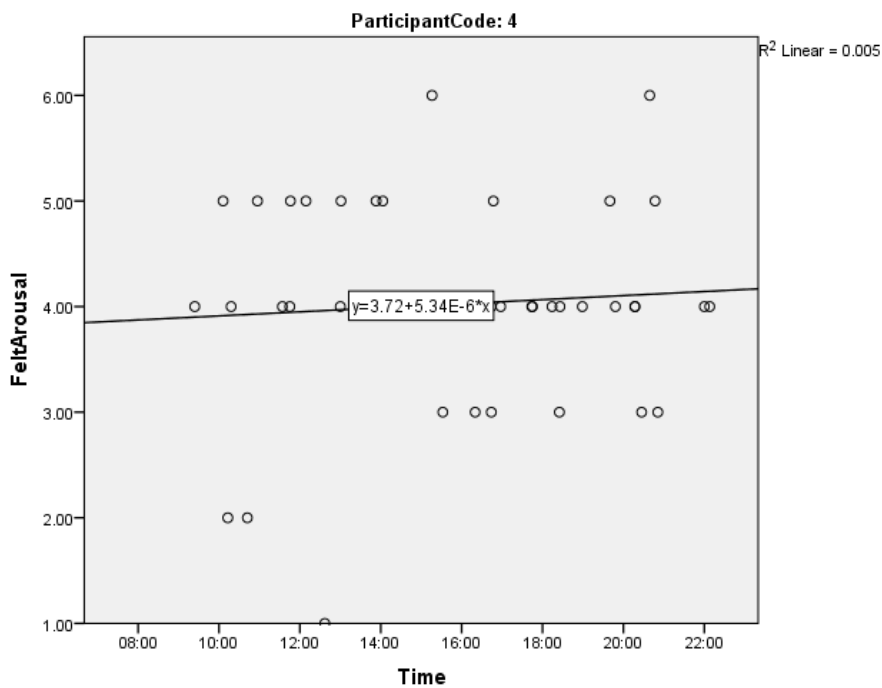


Figure 18: Scatterplot of Bivariate Pearson's Correlation Coefficient for Felt Arousal and Time

Participant 5

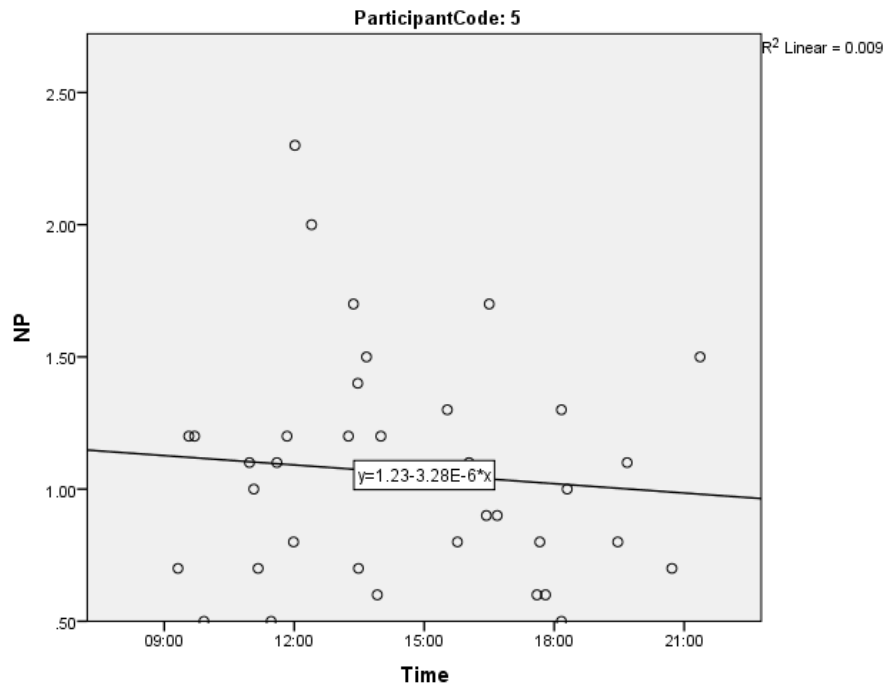


Figure 19: Scatterplot of Bivariate Pearson's Correlation Coefficient for NP and Time

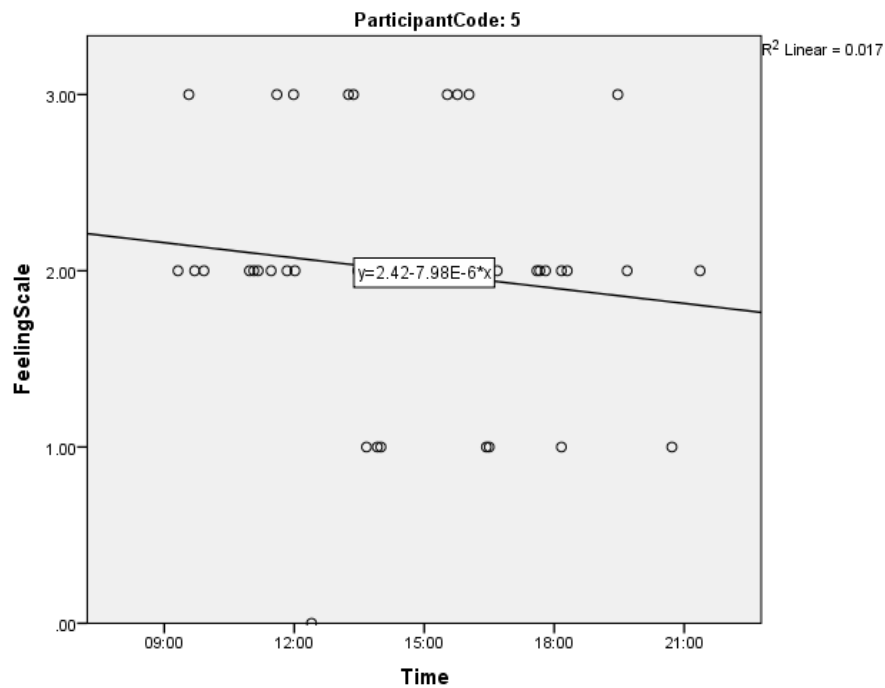


Figure 20: Scatterplot of Bivariate Pearson's Correlation Coefficient for Feeling Scale and Time

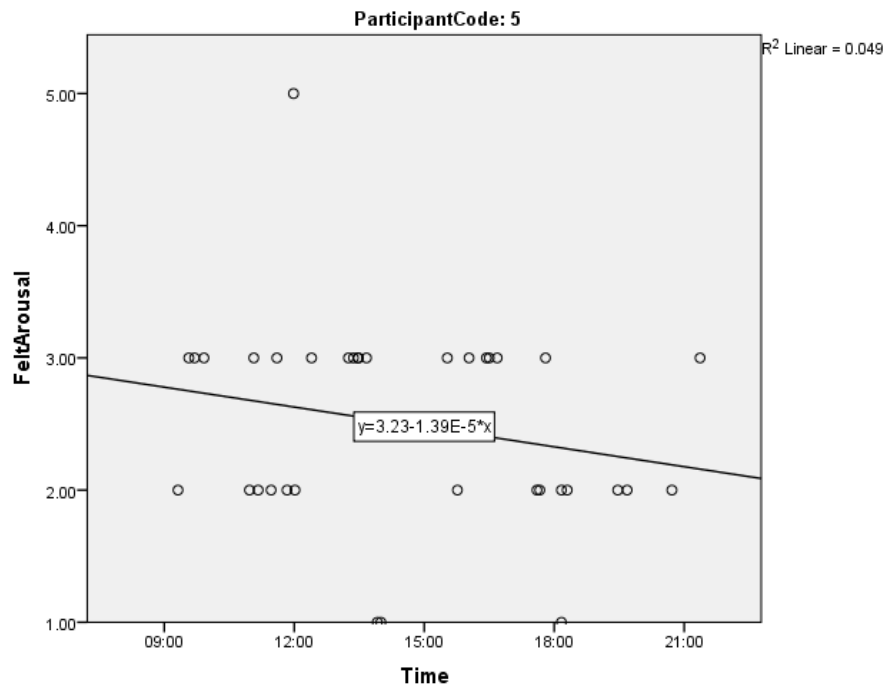


Figure 21: Scatterplot of Bivariate Pearson's Correlation Coefficient for Felt Arousal and Time

Participant 6

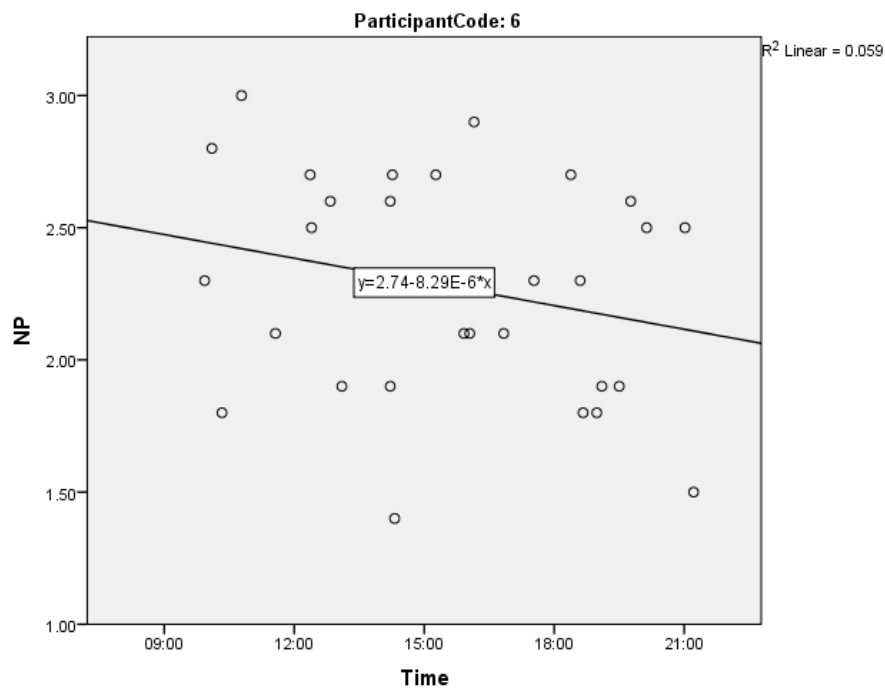


Figure 22: Scatterplot of Bivariate Pearson's Correlation Coefficient for NP and Time

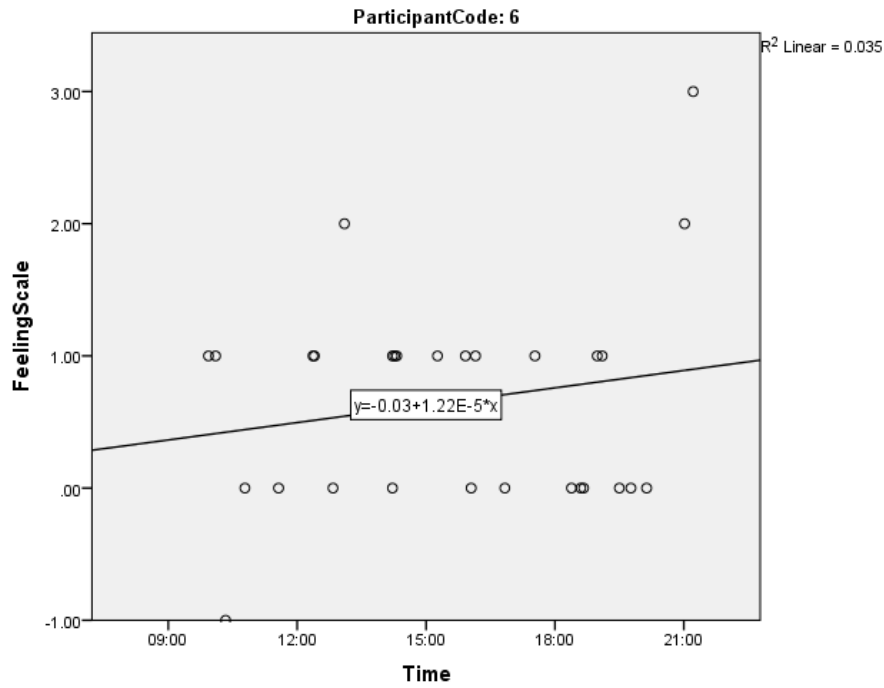


Figure 23: Scatterplot of Bivariate Pearson's Correlation Coefficient for Feeling Scale and Time

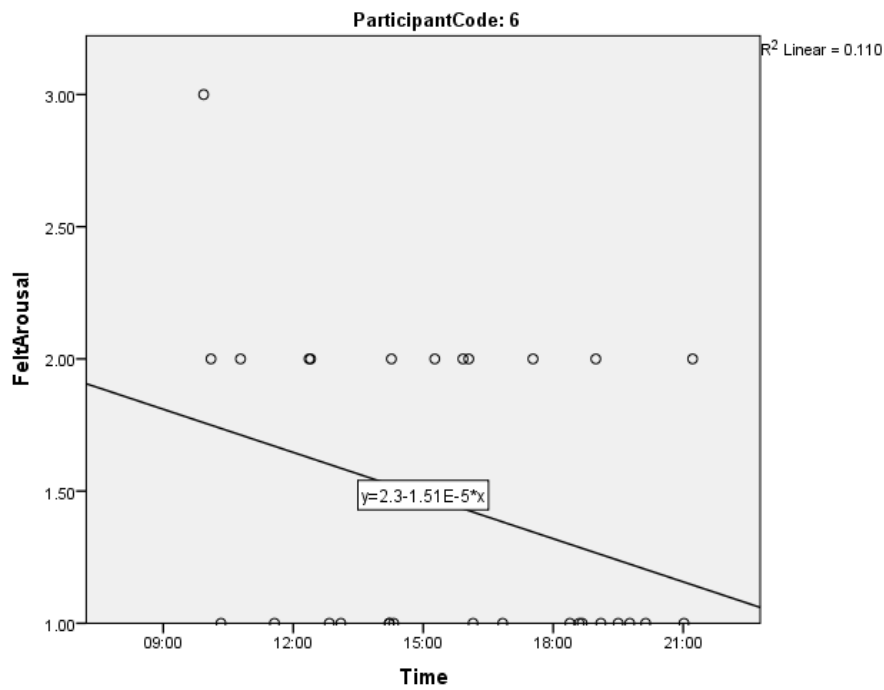


Figure 24: Scatterplot of Bivariate Pearson's Correlation Coefficient for Felt Arousal and Time