Effects of home-based electrical stimulation exercise on aspects of mood and quality of life

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EFFECTS OF HOME-BASED ELECTRICAL STIMULATION EXERCISE ON APSECTS OF MOOD AND QUALTY OF LIFE (127 pp.)

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The purpose of this investigation was to understand the effects of acute and chronic home-based electrical stimulation exercise on individuals with complete spinal cord injury (SCI). Ten individuals with SCI completed 25 total days of questionnaires including the Brief Assessment of Mood (BAM) for Total Mood Disorder (TMD) and Energy Index (EI), Positive and Negative Affect (PANAS), Personal Health and Depression–8 (PHQ-8), General Anxiety Disorder–7 (GAD-7), Long Term Physical Activity Questionnaire–SCI (LTPAQ-SCI), SCI Quality of Life Index (SCI-QLI), and visual analog scales for pain (VAS-P) and spasticity (VAS-S). On day 6 participants completed a bout of ESE. Participants then completed four weeks of five days per week of ESE. Participants completed all questionnaires on day one, day 6, day 15, and day 25 one-hour Prior, and before sleep. Participants completed the BAM and VAS for pain and spasticity only on days two through five, Day 1, Day 6, Day 16, and Day 25 upon wake (UW), one-hour prior (, immediately-post (IP), and before sleep (BS) on days 7-14, and days 16-24. Analysis of variance analyses were conducted, the results revealed no apparent benefits from home-based electrical exercise on mood, quality of life, or physical activity.

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CHAPTER I

INTRODUCTION

Spinal cord injuries (SCI) are physical insults upon the nerves of the spinal column that result in temporary or permanent loss of function (Eckert & Martin, 2017; Hachem et al., 2017). Many symptoms seen in SCI may also be secondary to neurological disorders such as multiple sclerosis and leukodystrophy and termed SCI Disorders (SCI) (McDonald & Sadowsky, 2002). Spinal cord injury is estimated to affect 17,730 new individuals each year (Jain et al., 2015) with non-traumatic SCI prevalence four-times greater than traumatic SCI (McDonald & Sadowsky, 2002). Chronic SCI often results in a myriad of negative health complications including sarcopenic obesity (Gorgey & Gater, 2007; Pelletier et al., 2016) loss of bone mineral density (Biering-Sørensen et al., 1990), loss of fat free mass (Giangregorio & McCartney, 2006), and reductions in cardiorespiratory endurance (Jacobs & Nash, 2004). Unfortunately, major depression and other mood disorders have also been observed in this population. Studies have shown depression occurs in individuals with SCI at a prevalence of 11% to 30% (Brazeau & Davis, 2018; Craig et al., 1996; Hoffman et al., 2011), compared to only 7% of abled bodied individuals (*2017 National Survey on Drug Use and Health: Methodological Summary and Definitions*, n.d.)

Physical activity (PA) and structured exercise for SCI remains significantly lower than able bodied individuals (Mainous et al., 2019). It is well established that participating in regular exercise is beneficial for increasing physical capacity, energy expenditure, mental health and reducing the risk of CVD, obesity, and type II diabetes in the SCI population (Bresnahan et al., 2019; Carek et al., 2011; DiCarlo et al., 1983; P. C. E. de Groot et al., 2003). Although therapeutic exercise can involve robotic or manually assisted training and functional stimulation,

upper arm ergometry is the most widely used form of exercise in this population. However, while upper body exercise is great for increasing cardiovascular fitness and upper body strength, it neglects the lower limbs.

Electrical stimulation exercise (ES) is a modality that can allow those with complete SCI to excite the muscles of the lower limb, and when performed in a prescribed and routine fashion, can minimize or reverse non-use muscle atrophy and vascular dysfunction inflicting this population. External electrical stimulation of muscle groups has also improved scores of depression, quality of life, physical function, and mental health in patients with cancer, congestive heart failure, and low back pain (Crevenna et al., 2006; Durmus et al., 2009; Karavidas et al., 2006), however there is no published data on the role of ES exercise on mental/mental health in those with SCI. Furthermore, ES exercise typically requires individuals to visit health/rehabilitation facilities and, due to SARS-CoV-2 (COVID-19) and Ohio's stay at home order, individuals are currently unable to access these facilities (DeWine et al., 2020) which will likely lead to increased emotional and mental stress as well as reduced physical activity.

Therefore, the overall purpose of this investigation is to determine the feasibility, adherence, and effectiveness of utilizing PowerDot, a new commercially available muscle stimulator for a home-based electrical stimulation exercise program for those with SCI. This study will include two separate aims. Aim 1 will assess how an acute bout of home-based ES exercise impact several aspects of mental health including mood, positive and negative affect, depression, anxiety, and quality of life. Aim 2 will assess how a 4-week intervention of home-based ES exercise influences those same aspects of mental/mental health. We hypothesize that after acute and chronic ES, individuals will have a reduced feeling of anxiety, depression, and

increases in feelings of happiness, and fulfillment. We also hypothesize that ES will be a safe and feasible modality of exercise for individuals with SCI. Results from this study may support future inclusion of home-based ES exercise for individuals with paralysis.

CHAPTER II

REVIEW OF LITERATURE

Spinal cord injury is a life-changing neurological assault with great impact physically, mentally, emotionally and socioeconomically (Alizadeh et al., 2019). There are an estimated 12,500 new cases of SCI each year in North America (Alizadeh et al., 2019; Hachem et al., 2017). The consequences of SCI depend on the severity and location of injury which leads to either complete or incomplete quadriplegia or paraplegia, respectively (Hachem et al., 2017). Individuals with SCI who are wheelchair users have an estimated 75% of their normal life expectancy (Shavelle et al., 2015), with the estimated life-time financial burden of $2.35 million per person (Hachem et al., 2017; Shavelle et al., 2015). Reduced self-efficacy, lower quality of life, and depression all affect this population (Khazaeipour et al., 2015; Middleton et al., 2007; Roshanaei-Moghaddam et al., 2009). There are numerous reports that suggest exercise can combat these conditions (Paolucci et al., 2018; Roshanaei-Moghaddam et al., 2009). However, a study of 70 individuals with SCI assessed physical activity participation via the Physical Activity Scale for Individuals with Physical Disabilities (Mat Rosly et al., 2018). Results indicated that 73% of the sample did not participate in moderate or vigorous leisure-time physical activity (LTPA), with “inaccessible facilities” as a top three barrier (Mat Rosly et al., 2018). Another large cross-sectional study (n = 695) resulted in 49.9% of individuals with SCI participating in 27.1 ± 49.4 minutes of LTPA a day, with the remaining 50.1% reported no LTPA at all (Ginis et al., 2010).

Cardiorespiratory Fitness

Following motor-complete SCI, individuals are unable to innervate any muscle tissue below the injury, reducing the total volume of muscle mass that can participate in physical

activity. For example, injuries at or above the sixth thoracic level (>T6) can affect neural control over cardiac and smooth muscle which would alter cardiovascular homeostasis (Furlan et al., 2003; Krassioukov et al., 1999). Typically arm cycle ergometry training is utilized for physical activity after SCI; unfortunately, systemic benefits to the muscle and vascular system is limited in the non-active limbs (Thijssen et al., 2009). It has also been reported that after SCI, there are rapid reductions in femoral artery diameter and blood flow of 50% and 40%, respectively (Hopman et al., 1994; Nash et al., 1996). These processes of deconditioning can become deleterious and lead to maladaptation of the cardiorespiratory system. A retrospective cross-sectional study of 437 veterans with SCI showed that 57% had metabolic syndrome, 76.7% had a BMI > 22 $kg{\cdot}m^2$, 55.1% were currently treating hypertension and had adjusted odds ratio of 2.72 for development of cardiovascular disease (Cragg et al., 2013; Gater et al., 2019).

Musculoskeletal fitness and loss of mobility

Maintenance of muscle mass and bone density below the site of injury becomes profoundly challenging for individuals with SCI. Immediate and full denervation of muscle tissue below the site of injury leads to rapid muscular atrophy and reduction in bone density (Llewellyn-Smith et al., 2007; Wang et al., 2016; Xia et al., 2017). Specifically, Garland and colleagues reported a 30% reduction in bone mineral density (BMD) 18 months post-injury (Garland et al., 2008). Wall et al. (2013), reported a significant reduction in muscle mass and strength as well as an increase in molecular catabolic signaling process after only 5 days of muscle disuse. Studies have shown that within 3-weeks post SCI thigh girth is reduced by 50% and muscle bulk is reduced by 40% (Maïmoun et al., 2011; Ooi et al., 2012). Further investigations showed that within 6-months of SCI there is a reduction in cross-sectional area (CSA) of the quadriceps, hamstrings, and adductor muscle groups by 16%, 14%, and 16%

respectively (Kannisto et al., 1998). Furthermore, this muscle atrophy likely contributes to increased risk of diabetes considering skeletal muscle is the body's largest glucose consumer by mass, accounting for approximately 80% of non-insulin stimulated glucose uptake (Thiebaud D et al., 1982). Taken together, these two factors illustrate the importance of preserving lean muscle mass in persons with spinal cord injuries.

Previous studies have indicated a positive correlation between muscle cross-sectional area (MSCA) and the ability to produce force (Bochkezanian et al., 2018; Tonson et al., 2008; Zengin et al., 2017). A typical method to increase MSCA is through high-intensity muscle contraction, which have proven to benefit long-term health and quality of life in clinical populations. However, paraplegics with motor complete SCI are constrained to participating in volitional upper body exercise only. This includes upper body resistance training and arm ergometry. Although, as previously stated, blood flow dynamics are not altered in the inactive limbs making systemic benefits challenging. In addition, investigators who have conducted survey research have reported up to half of adults with SCI have shoulder pain, often lasting over longer than one year (Van Straaten et al., 2017). This may be an important reason why individuals with motor complete SCI are so apt to remain physically inactive and not participate in traditional exercise (Levi et al., 1995).

Exercise, Mental health and Depression

Depression is a major disability within the United States, with 72.3% of people meeting criteria but not receiving treatment (Kohn et al., 2004). In addition, it has been shown that in any given 2-week period, up to 8.1% of individuals 20 years and older experience depression (Brody, 2018). While women are more likely to develop depression, they are also more likely to seek psychiatric treatment compared to men (Addis & Mahalik, 2003). This poses a potential disparity

as the overwhelming majority of new SCI cases (approximately 80%) are male (*National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance*, 2019). The reduced lifespan due to spinal cord injury may be further exacerbated as individuals with depression have increased incidence and mortality of cardiovascular disease (Belvederi Murri et al., 2019). Also, a large financial burden accompanies depression. From 2005 to 2010, there was a 21.5% increase in to the cost associated with major depressive disorders (Greenberg et al., 2015), and it's expected to cost an estimated 16.1 trillion USD over the next 20 years (Bloom et al., 2012).

In abled-bodied individuals, physical activity has been gaining attention as a non-pharmacological means of treating major depression and emotion regulation (Brown et al., 2013; Giles et al., 2017). A 10-year cohort study with 424 healthy participants investigated the relationship between PA, exercise coping, and depression and concluded that PA was correlated with a reduced global depression score (Harris et al., 2006). A hallmark study concluded that patients themselves viewed PA as beneficial for reducing depression (Searle et al., 2011), although the exact mechanisms underlying these benefits as well as the required intensity and modality of exercise required is not clear (Searle et al., 2011). Another investigation compared a walking intervention (20 to 40 minutes per day, 3 days per week for 6 weeks) to either a social support group or a wait-list group on the effectiveness of treating depression symptoms. The investigators concluded that the exercise group alleviated overall symptoms of depression and was more effective than the other two cohorts (McNeil et al., 1991). Data also suggests that exercise benefits on mental health may be long lasting. DiLorenzo and colleagues (1999) assessed the impact of either 24-mins of interval or 48-mins of steady state cycling both at 70-85% of peak, four times per week on heart rate reserve on anxiety, depressive symptoms, mood, and self-concept in able-bodied individuals. After 12-weeks of training both exercise groups had

improved scores compared to the control group, however in agreeance with Searle et al. (2011) the exercise protocols resulted in similar improvements (DiLorenzo et al., 1999). Tawashy and colleagues assessed the intensity and mode of physical activity in those with SCI on depression via the 10 item Centre for Epidemiological Studies-Depression scale (CESD-10). Interestingly those who participated in higher amounts of mild physical activity correlated with lower levels of depression and pain (Tawashy et al., 2009).

Along with depression, anxiety has been shown to have a lifetime prevalence of 30-35% for able-bodied 18-60 years old in the United States (Carmin & L. Ownby, 2010). A recent study of individuals with SCI indicated increased incidence of anxiety disorders (19.3% vs 14.1%) when compared to adults without SCI (Peterson et al., 2020). Even among this healthy able-bodied population, anxiety is associated with behaviors such as physical inactivity and poor diet (Jonas et al., 1997; Bonnet et al., 2005). Conversely, exercise, being structured physical activity, may be a beneficial tool for treating anxiety. Berger and Owen (1998) investigated the influence of 20-minutes of treadmill exercise at either 55, 75, or 79% of age-adjusted maximum heart rate on anxiety in 91 college students. Each participant completed all three trials separately. Exercise, regardless of intensity, improved all subscales of the Profile of Mood States (Berger & Owen, 1998). Lastly, men and women with complete and incomplete spinal cord injuries have shown a strong positive correlation ($r = 0.75$, $p < 0.05$) between level of physical activity and quality of life (Stevens et al., 2008). Clearly there is an important link between physical activity and well-being, but there also seems to be lacking participation of individuals with SCI in LTPA.

Lastly, there is a complex entanglement of pain, depression, and anxiety. Individuals with chronic pain are three times as likely to develop symptoms of anxiety or depression. Moreover, those with anxiety or depression are three times as likely to develop chronic pain

(Fishbain et al., 1986) with up to 85% of patients with chronic pain are also affected by severe depression (Bair et al., 2003). Exercise in various forms have shown to be self-reported by 69% of individuals in a survey study to help reduce pain on a scale of four out of 10 (Cardenas & Jensen, 2006). Therefore, the potential use of exercise as a means to mitigate depression and anxiety or chronic pain may have important uses as there seems to be a complex involvement of both in the development of each complication.

Electrical Stimulation

This disruption of the corticospinal tract due to SCI renders the tract unable to communicate neuronal impulses to the peripheral muscle tissue (Javed & Lui, 2019). Electrical stimulation (ES) utilizes an electrical charge applied directly to the paralyzed muscle to initiate a muscle contraction. Functional electrical stimulation has been utilized for populations such as SCI, multiple sclerosis, stroke and seniors (Barrett et al., 2009; Eraifej et al., 2017; Hasnan et al., 2013; Kern et al., 2014). A systematic review from 2014 indicated that although the electrical stimulation parameters have yet to reach a unified consensus (Burke et al., 2016) the typical adjustable parameters for stimulation include wave form, frequency, pulse width, and amperage. Of the twelve studies assessed for the systematic review, 10 of the 12 utilized biphasic waveforms, with a mixture of symmetric impulses, symmetric constant impulses, and rectangular wave pulses (Burke et al., 2016). Frequency utilized ranged from 35 to 100 Hz with pulse width occurring anywhere from 200 to 400 μs (Burke et al., 2016). While maximal tolerable intensity ranged from 15 mA up to 110 mA, this large range is most likely due studies utilizing patients with sensation (i.e. stroke or sepsis) compared to individuals with no sensory feedback (i.e. spinal cord injury) (Burke et al., 2016).

Electrical Stimulation – Physiological and Psychological Benefits

Electrical stimulation exercise may be an acceptable modality for individuals with SCI to participate in meaningful and beneficial exercise for the paretic limbs. Helmkamp and colleagues performed a hallmark study assessed the training effects of 36 sessions of ES cycling over 12 weeks for 30-minute sessions in participants with SCI. Their results indicted significant increase in cardiac output (Q) from pre to post-training in quadriplegics and significant changes in VO_2 from rest compared to submaximal exercise in both quad and tetraplegics (Helmkamp, 1995). A more recent study from 2016 utilized a RT-300 ES cycling for 12-weeks of training three times a week on individuals with SCI. From the first three bouts to the last three bouts, there was a significant increase in distance achieved (16.03 ± 8.29km vs. 34.10 ± 6.51km; respectively) and femoral artery pulse volume (PV) (4.25 ± 0.81mL vs. 5.69 ± 2.06mL; respectively) (Allison et al., 2016). A youth study (5 to 13 years old) assessed VO_2 and fasting lipid profile in either ES cycling, passive cycling, or noncycling control with electrical stimulation therapy. Their results indicted a significant positive change in the ES cycling group (16.2% ± 25%) when compared to the passive cycling (-28.7% ± 42%) (Johnston et al., 2009).

In addition to the physical benefits, the influence of ES on mental health has also been investigated. Karavidas and colleagues assessed 30 minutes a day, 5 days per week for 6 weeks of quadricep and gastrocnemius electrical stimulation in 30 congestive heart failure patients (Karavidas et al., 2006). When comparing the ES exercise group (n = 20) to the placebo (n = 10), the ES group was associated with decreased scores on the Beck Depression Inventory (BDI) and Zung self-rating depression scale (SDS) with an increase in the physical limitation and quality of life questionnaire (Kansas City Cardiomyopathy Questionnaire) (Karavidas et al., 2006). A similar case study on a 47 year-old patient with lung cancer utilized gluteal and knee extensor stimulation of 20 60-minute sessions (30 minutes dedicated to each the gluteal and quadriceps

stimulation) for 4 weeks (Crevenna et al., 2006). A SF-36 health survey (generally accepted questionnaire for assessing health-related quality of life) was administered before and after the training session. There were improvements in the categories of: physical functioning, mental health, role-emotional, and general health. After the intervention, these improved scores reflected those of an able-bodied healthy 41-50 year old (Crevenna et al., 2006). Durmuss and colleagues (2009) assessed the effects of ES for able-bodied persons with chronic low back pain. Participants were split into one of two groups, group one received ES and exercises, while group 2 (control) received only exercises. A symmetric biphasic ES was utilized on the erector spinae and the obliquus externis abdominis muscles when in the prone and supine position; respectively, for 15 minutes while in each position (Durmus et al., 2009). Outcome measures included quality of life (via the SF-36) and depression (via Beck depression inventory (BDI)). Results indicated that both groups had improvement in QOL, and depression scores compared to baseline. Interestingly, besides depression and social function (a subset of the SF-36) the experimental group resulted in greater improvements after treatment compared to control (Durmus et al., 2009). Unfortunately, to my knowledge, there is no study that has investigated the effect of electrical stimulation exercise on mental health in individuals with SCI.

Conclusion

There has been clear evidence that after sustaining a SCI, there is decreased mental and mental health (Brazeau & Davis, 2018; S. Craig et al., 1996; Hoffman et al., 2011). Fortunately, there is clear evidence of the benefit of voluntary exercise on physical and mental health in all populations (Brown et al., 2013; DiLorenzo et al., 1999; Giles et al., 2017; McNeil et al., 1991; Searle et al., 2011; Stevens et al., 2008; Tawashy et al., 2009). Unfortunately, individuals with disabilities are far more apt to not participate in PA due to a myriad of barriers, which potentially

increase the possibility of reduced mental health (Lui & Hui, 2009). There is also clear evidence that ES exercise may also help to promote physical, mental, and mental health in a wide array of populations (Allison et al., 2016; Crevenna et al., 2006; Durmus et al., 2009; Helmkamp, 1995; Johnston et al., 2009; Karavidas et al., 2006). However, there appears to be a lack of research focused on the effects of ES exercise on mental and mental health in individuals with SCI. Even more so, with the barriers they face to exercise, there is a clear void of information on home-based ES exercise programs and their effect on mental and mental health. This lack of understanding needs to be explored as it is very likely that during the pandemic mental and mental health are more vulnerable than ever. Furthermore, those with SCI are likely unable to access clinics or gyms for their typical exercise. We hypothesis that an acute bout of home-based ESE will have positive outcomes on scoring of the mood, anxiety score, pain, and spasticity. Additionally, we hypothesize that an acute bout will not have a significant positive affect on positive or negative affect, depression scores, or quality of life. Lastly, we hypothesize that four weeks of home-based ESE will have significant positive outcomes on mood, positive and negative affect, depression, anxiety, quality of life, pain, and spasticity. Therefore, the first specific aim of this research study are as follows:

Specific Aim 1: Determine if an acute bout of home-based ESE has significant positive impacts on mood, positive and negative affect, anxiety, depression, quality of life, pain, and spasticity.

Specific Aim 2: Determine if chronic home-based ESE has significant positive impacts on mood, positive and negative affect, anxiety, depression, quality of life, pain, and spasticity

CHAPTER III

METHODOLOGY

A total of 12 individuals (35 ± 11 yrs.) with complete spinal cord injury were recruited to participate in this experimental study. Inclusion criteria included spinal cord injury classification of A or B as determined by the American Spinal Association Impairment Scale (ASIA), post-injury of at least one year, and 18-70 years of age. Exclusion criteria included evidence of mower motor neuron injury, internal pacemaker or defibrillator, active infection or disease, history of autonomic dysreflexia, excessive spasticity, pressure wounds, cardiovascular or hematological disease, unable to speak English, inability to utilize upper limbs to place electrodes, and no access to smart device or reliable internet connection. Participants were recruited from the University and surrounding areas. After an explanation of all procedures, risks, and benefits, each participant provided their written informed consent prior to participation in this study. The research protocol and the informed consent document were approved by the Kent State University Institutional Review Board prior to participant enrollment (Approved February 16, 2021). One adverse event was reported, whereby a participant reported a small wound on the thigh after use of equipment. Further investigation into the event revealed faulty deposable reagent use from the manufacturer. The adverse event was reported to the Institutional Review Board. Furthermore, two participants dropped out due to medical reasons and were not included in the final analysis of this study.

Power was calculated using G*Power and the procedures described by Beck (2013). Analyses based on the mean differences in the brief assessment of mood by Shearer et al. (2015) indicated that a total sample size of 10 would produce a statistical power ($1 - \beta$) of 0.80 at an alpha level of 0.20. Additional a priori power analyses were conducted to confirm sample size

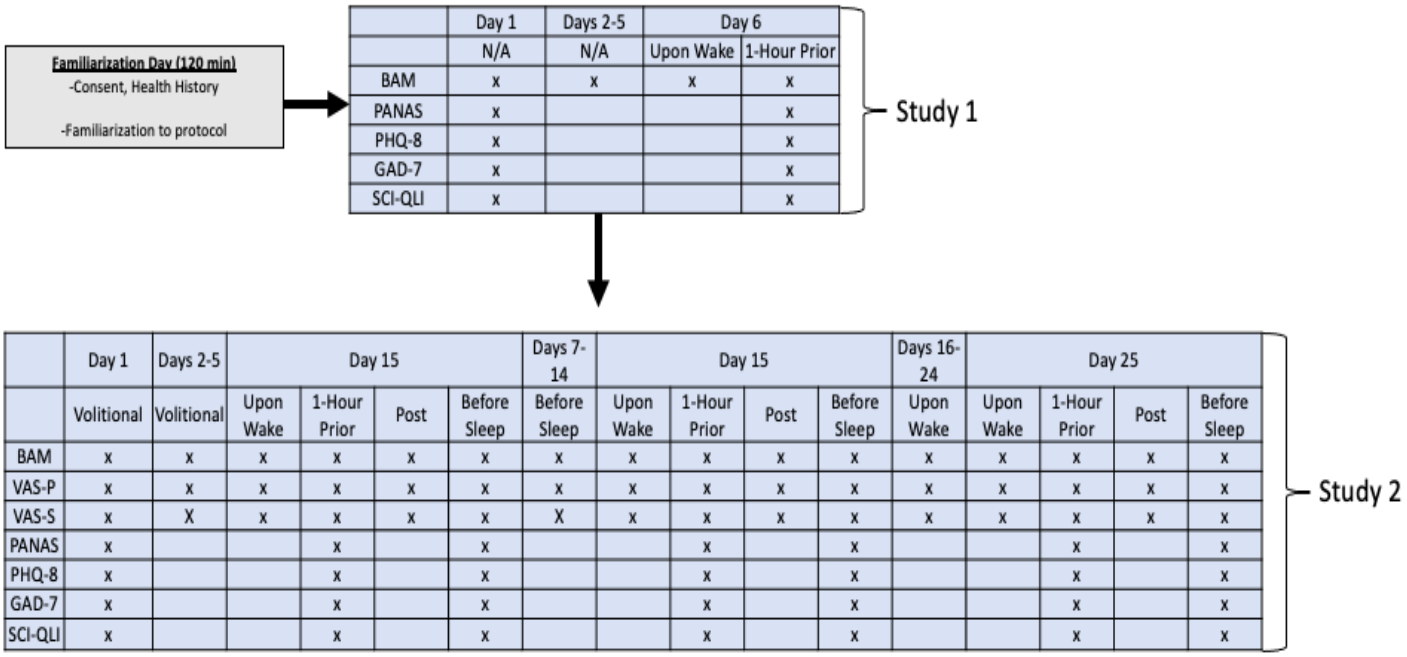
estimation. This data was used to estimate sample size a priori for the present study due to the similarities in study design and outcome variables.

Study Design

Testing took place over 26 sessions for each participant. All required equipment was either mailed or delivered to the participants. Session one consisted of providing informed consent, written consent and medical and health history. Experimental days one through five consisted of only completing questionnaires. Days one through five were used as a run-in period as to attempt to limit type 1 error. This allowed for researchers to obtain a baseline for each individual prior to the addition of the ESE program so participants could serve as their own controls. Day six marked the first day of a 20 session home based ESE program. Exercise sessions were required to be completed each day Monday through Friday for a total of five ESE session per week. Experimental days 6, 16, and 26 consisted of ESE and four sets of questionnaires throughout the day. An overview of the study design can be found in Figure 1.

Figure 1

Study Design



	Day 1	Days 2-5	Day 6	
	N/A	N/A	Upon Wake	1-Hour Prior
BAM	x	x	x	x
PANAS	x			x
PHQ-8	x			x
GAD-7	x			x
SCI-QLI	x			x

	Day 1	Days 2-5	Day 15				Days 7-14	Day 15				Days 16-24	Day 25			
	Volitional	Volitional	Upon Wake	1-Hour Prior	Post	Before Sleep	Before Sleep	Upon Wake	1-Hour Prior	Post	Before Sleep	Upon Wake	Upon Wake	1-Hour Prior	Post	Before Sleep
BAM	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
VAS-P	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
VAS-S	x	X	x	x	x	x	X	x	x	x	x	x	x	x	x	x
PANAS	x			x		x			x		x			x		x
PHQ-8	x			x		x			x		x			x		x
GAD-7	x			x		x			x		x			x		x
SCI-QLI	x			x		x			x		x			x		x

Procedures

During initial patient contact, participants were required to read and sign an informed consent, followed by completing a medical and health history questionnaire. Next all participants were instructed on proper set-up and use of the electrical stimulation device (PowerDot, Carlsbad, California, USA). In brief, the electrical stimulation device requires two electrodes to be placed either over the inferomedial and inferolateral anterior thigh superior to the patella for knee extension or inferomedial and inferolateral posterior thigh just superior to the popliteal fossa for knee flexion and the third electrode placed superior to each set of electrodes respectively as per manufacturers recommendation which served as a ground. During the ES exercise session, stimulation of the quadriceps for 24 minutes was completed first and then on the hamstrings for an additional 24 minutes. For their exercise sessions subjects utilized a pre-programmed ES protocol which consisted of 5 seconds of symmetrical biphasic stimulation at 40 Hz, with a 208 μsec pulse width for contractions followed by symmetrical biphasic pulse of 4 Hz, five seconds long for rest. This cycle of stimulation and rest repeated for 24 minutes for each muscle group (48 minutes of total exercise). The intensity, which was based on tolerance and visual feedback of an active muscle contraction, ramped up over the first 2 seconds and ramped down over the last 0.5 seconds of each 5 second stimulation period. As this was a home-based exercise program, and adherence is a dependent variable, there was no control set in place for completion time of prescribed exercise program.

Next participants were instructed on how to properly complete the daily questionnaires (described below) on their personal use electronic devices via Qualtrics (Povo, Utah, USA). In brief, participants received an email link for all required time points which were mailed out at 5 a.m. each day and labeled explicitly for required time of completion. Participants scheduled with

the investigator an approximate time they would complete daily exercise training which subsequently influenced when they would complete the questionnaires. On experimental day one, participants completed all questionnaires (BAM, PANAS, PHQ-8, GAD-7, SCI-QLI, VAS-Pain, VAS-Spasticity). On days two through five, participants will only complete the BAM and the VAS for pain and spasticity. No exercise sessions were completed during these first five days. On the sixth experimental day (which always began on a Monday) participants completed four sets of questionnaires. Upon wake (UW) and immediately post-exercise (IP), participants completed the BAM and VAS for pain and spasticity. One-hour prior (1H) to ESE and before bed (BS), participants completed the BAM, PANAS, PHQ-8, GAD-7, SCI-QLI, and VAS for pain and spasticity. Experimental days 11 and 21 were identical to experimental day six. Conversely, experimental days 7-10 and 12-20 participants only completed ESE at the previously determined timepoint and the BAM and VAS for pain and spasticity. For completion for quality control Participants were asked to self-report if they did not complete a questionnaire or changed their typical time. This was monitored by the research team through Qualtrics response system.

Questionnaires

All questionnaires utilized in this investigation are listed below. These questionnaires were utilized as they are specific to the aims of the study. Additionally, they are appropriate for the population of spinal cord injury.

Brief Assessment of Mood (BAM)

The brief assessment of mood (BAM) is an abbreviated version of the Profile of Mood States (Searight & Montone, 2017). The BAM consists of six mood adjectives: angry, vigor, fatigued, depressed, confused, and tense (Dean et al., 1971). These six items are rated along a 5-

point Likert scale with 1 standing for nothing at all and 5 signifying extremely, with participants responding how they feel in the moment at the time of completion. To calculate TMD, the Vigor score is subtracted from the sum of the five other mood items, with higher scores indicating higher TMD. The EI is assessed as a ratio of vigor to fatigue, with a higher score indicating a greater level of recovery. Importantly, the EI is more informative than Fatigue and Vigor scores alone as it assesses the opposing effects of both constructs. Initial validation of the BAM TMD on college students (n = 621), BAM TMD scores were highly correlated with profile of mood sates TMD scores (r = .88, $p < 0.001$) along with the Cronbach's coefficient alpha for the BAM TMD being acceptable (a = .75) (Dean et al., 1971). Lastly, EI has been shown to be correlated to changes in neuroendocrine response to the Ironman competition (Odagiri et al., 1996).

Positive and Negative Affect Schedule (PANAS)

The positive and negative affect schedule is a self-reported assessment that consists of various words and synonyms that describe feelings and emotion (Magyar-Moe, 2009). The PANAS has been adopted for use as a self-reported measure in community and clinical contexts (Merz et al., 2013). The PANAS allows users to respond to 64 items utilizing a 5-point Liker scale with 1 signifying "slightly or not at all" up to 5 "extremely". Clinical and non-clinical investigations have shown PANAS to be a valid assessment (Merz et al., 2013). It has been states that the PANAS assess both positive and negative emotions for users from week-to-week as they engage in their life (Magyar-Moe, 2009), making this an appropriate assessment to be conducted for the chronic study.

Personal Health Questionnaire Depression Scale (PHQ-8)

This questionnaire utilizes eight items to assess depressive studies, originally designed for large clinical studies (Kroenke et al., 2009). The questionnaire asks the participant to assess how

they feel over the past two weeks for each of the eight items. The participant answers on a 4-point Likert-scale with 0 signifying “not at all” and 3 signifying “nearly every day”. The assessment and subsequent prevalence of depression is defined by a PHQ-8 score greater than or equal to 10 (Kroenke et al., 2009). It has been shown that the PHQ-8 can be successfully utilized to define current depression in the general population (Kroenke et al., 2009).

General Anxiety Disorder (GAD-7)

The GAD-7 was originally developed to allow a brief, self-reported scale to identify cases of general anxiety disorder (GAD). The GAD-7 requires the participant to answer 7 items pertaining to how they have felt over the last two weeks (Spitzer et al., 2006). Scoring of 5, 10, and 15 are cut-off points for mild, moderate, and severe anxiety, respectively. When the cut-off score of 10 is used, the GAD-7 has a 89% sensitivity to detects GAD (Spitzer et al., 2006). It has also been shown the GAD-7 is a valid tool for screening for GAD (Spitzer et al., 2006).

Spinal Cord Injury Quality of Life (SCI-QLI)

The SCI-QLI is a quality-of-life questionnaire specifically designed for individuals with spinal cord injury. Previous work was completed to develop a revised version, which includes 37 items in each of two sections: one assessing satisfaction with life aspects and the other assesses the importance of those aspects. Each of these questions are assessed with a six-point bar graph scale ranging from 1 (not at all satisfied/important) up to 6 (very satisfied/important) (May & Warren, 2002). The SCI-QLI has been shown to have clinical validity for a SCI population with Pearson correlations of $r = 0.99$ (Jain et al., 2007; May & Warren, 2002).

Leisure Time Physical Activity Questionnaire – Spinal Cord Injury (LTPAQ-SCI)

The LTAQ-SCI is a questionnaire to assess leisure time physical activity specifically designed for individuals with SCI. Compared to the Physical Activity and Disability Scale

(PADS) (Rimmer et al., 2001) Physical Activity Scale for Individuals with Physical Disabilities s(PASIPD)(S. de Groot et al., 2010) the LTPAQ-SCI it assesses different types of LTPA at varying intensities. In addition, the LTPAQ-SCI does not require the time nor a trained review to complete the assessment (Martin Ginis et al., 2012) while mirroring the structure of the brief self-report measures of LTPA in able-bodied individuals such as the Godin Leisure Time Exercise Questionnaire (Godin & Shephard, 1985) and the short version of the International Physical Activity Questionnaire.(C. L. Craig et al., 2003). Additionally there was moderate to strong correlations between the LTPAQ-SCI and the PARA-SCI measures of LTPA (Martin Ginis et al., 2012).`

Statistics for Study 1

Statistical analyses were performed using SPSS software (IBM Corporation, Amonk, NY, USA). All questionnaires listed previously were assessed at each individual time-point in which they were presented to participants. Therefore, the BAM, VAS-Pain, and VAS-Spasticity was assessed at nine different data points (each day during the run in and four times during day 6: upon wake (UW), one-hour prior (1H), immediately-post (IP), and before sleep (BS)) and all remaining variables were assessed on day one, day 6 1H and day 6 BS. Data was first assessed for homogeneity with Levene's test. In the event of a significant Levene's test data was ran via a one-way analysis of variances (ANOVA) and significance was assessed via Welch Tests. In event of a significant main effect, post-hoc analysis was done via Games-Howell as equal variances is not assumed. If Levene's test failed to reach significance data was assessed via univariate analysis of variance. In the event of a significant main effect, post hoc least significant differences pairwise comparisons were completed. Lastly, in the event of multiple variables

having significance on a single day, a correlation was ran and reported with as a Perason's correlation coefficient. All data are expressed as mean ± standard deviation (SD).

Statistics for Study 2

Statistical analyses were performed using SPSS software (IBM Corporation, Amonk, NY, USA). The BAM and VAS-P and VAS-S were averaged on days two through five, 7 through 14, and 16 through 24 and analyzed as 3 individual timepoints. All other questionnaires were assessed individually at each time point in analysis. Therefore, the BAM, VAS-P, and VAS-S was analyzed at 16 timepoints while remaining data was analyzed at seven timepoints. All data will first be assessed for homogeneity with Levene's test. In the event of a significant Levene's test data was ran via a one-way analysis of variances (ANOVA) and significance was assessed via Welch Test. In event of a significant main effect, post-hoc analysis was ran via Games-Howell as equal variances is not assumed. If Levene's test fails to reach significance, data was assessed via univariate analysis of variance. In the event of a significant main effect, post hoc least significant differences pairwise comparisons were completed. Adherence was expressed as a percentage. This was assessed via simple average of individual adherence percentage as expressed by division of sessions completed by sessions prescribed (20). All data are expressed as mean ± standard deviation (SD).

CHAPTER IV

STUDY 1

Acute effects of home-based electrical stimulation exercise on various mood states and quality of life.

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Introduction

Spinal cord injury (SCI) often result in permanent loss of muscle function, dependent upon location of injury (Eckert & Martin, 2017; Hachem et al., 2017). Currently, approximately 288,000 persons living with SCI in the United States, with 20.2% and 11.5% classified as either complete paraplegia or tetraplegia, respectively (*National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance*, 2019). Previous reports indicate depression occurs in individuals with SCI at a prevalence of 11% to 30% (Brazeau & Davis, 2018; Craig et al., 1996; Hoffman et al., 2011). A cross-sectional investigation of 134 adults with SCI reported 49.3% having mild to sever depression as defined by the Beck Depression Inverntory (Khazaeipour et al., 2015), compared to only 4.7% of abled bodied individuals (Clarke, 2019). Anxiety incidence also affects this population disproportionately (19.3% vs. 14.1%; SCI and able-bodied, respectively) (Peterson et al., 2020).

Quality of life (QOL) is an important measure to consider especially when the goal of treatment is centered around chronic disability (McGee, 2001). Reductions in physical fitness for this population may become a barrier to autonomy following a SCI (Anneken et al., 2010; Noreau & Shephard, 1995). Those who participate in physical activity report better quality of life in domains of physical, psychological and social contexts (Anneken et al., 2010; Tasiemski et al., 2000). Additional potential health benefits include stress relief, improvement in mood, increased energy and stamina, reduced tiredness and increased mental alertness have been promoted for all individuals (Sharma et al., 2006), with higher physical activity correlating to lower anxiety and depression scores in individuals with SCI (Kim et al., 2020). Unfortunately, in the SCI population barriers to exercise such as perceived low return on physical investment, lack of accessible facilities, transportation, and fear of injury pose potential hardships for this population

to participate in meaningful exercise (Gorgey, 2014; Kehn & Kroll, 2009), and adhere to exercise programs. Interestingly, it has been reported that individuals with SCI adhered to a home-based electrical stimulation cycling exercise program by 71.7% (Dolbow et al., 2012) compared to 35% (Schoenborn & Adams, 2010) of abled bodied and 48% of at-risk individuals (Saida et al., 2017).

Electrical stimulated exercise (ESE) has been utilized for individuals with complete SCI and other disabilities to help improve physical well-being (Allison et al., 2016; Bauman et al., 2016; Bélanger et al., 2000; Bersch et al., 2015; Bochkezanian et al., 2018; Burke et al., 2016; Coquart et al., 2016; Crevenna et al., 2006; Helmkamp, 1995; Kern et al., 2014; Natsume et al., 2015). For SCI patients, ESE allows the innervation of paralyzed musculature, which are typically otherwise sedentary. In patients with congestive heart failure, 30 minutes a day of ESE of the bilateral quadriceps and gastrocnemius muscles correlated to improvements in depression and quality of life (Karavidas et al., 2006). A similar case study of a patient with lung cancer utilized ESE for bilateral gluteal and knee extensor muscles for 4 weeks of 20 sessions which resulted in improvements of physical functioning and mental health via the SF-36 health survey (Crevenna et al., 2006). In able-bodied individuals with chronic back pain, ES resulted in improvements in quality of life and depression compared to baselines using the SF-36 questionnaire (Durmus et al., 2009). Combined ESE with volitional upper body exercise has also shown benefits to brief assessments of mood in patients with SCI and multiple sclerosis (Donia et al., 2019)

Therefore, the purpose of this study is to assess the feasibility of an acute bout of home-based ESE program and the subsequent effects on feelings of anxiety, depression, quality of life, pain, and spasticity. We hypothesize that an acute bout of home-based ES will have positive

effect on total mood disturbance (TMD) and energy intake (EI) via the brief assessment of mood (BAM) questionnaire, anxiety via the general anxiety disorder (GAD-7), and pain and spasticity assessed via visual analog scales (VAS). We also hypothesize that this single bout of home-based ES exercise will not have any effect on positive and negative affect schedule (PANAS), personal health questionnaire depression scale (PHQ-8) and spinal cord injury quality of Life 23 (SCIQLI-23).

Materials and Methods

We recruited 10 individuals with C4-T10 level SCI classified as motor complete by the American Spinal Injury Association Impairment Scale (ASIA A or B) (Marino et al., 2003). Participants were post-injury by at least 1 year (average 5.2 ± 9.2 years) post-injury and between 20-54 years of age. Descriptive characteristics about participants can be found in Table 1. Exclusion for participation in the study includes evidence of lower motor neuron injury, internal pacemaker or defibrillator, active infection or disease, history of autonomic dysreflexia, unable to speak English, no access to smart device or reliable internet connection, and severe reaction to electrode adhesive. All participants had a history of using ES. All participants that were currently participating in ESE (n = 3) ceased activity for one week prior to the study and for the duration of the study. Participants that were completing non-ESE were informed to continue to complete their routine exercises (n = 9). The research protocol and the informed consent were approved by the University's Institutional Review Board.

Power was calculated using G*Power and the procedures described by Beck (2013). Analyses based on the mean differences in the brief assessment of mood by Shearer et al. (2015) indicated that a total sample size of 10 would produce a statistical power ($1 - \beta$) of 0.80 at an alpha level of 0.05. Additional a priori power analyses were conducted to confirm sample size

estimation. This data was used to estimate sample size a priori for the present study due to the similarities in study design and outcome variables.

Table 1

Participant Characteristics

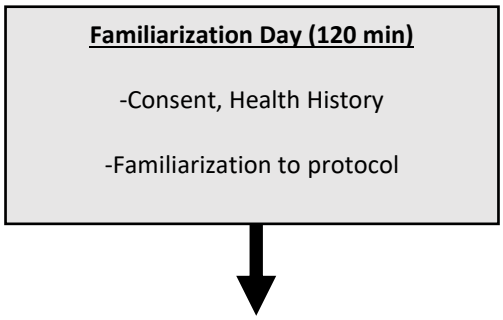
SUBJECT	YEARS SINCE INJURY	LEVEL OF INJURY	ASIA GRADE
1	4.6	T10	A
2	2.1	C4-C6	B
3	1.3	T8	B
4	3.8	C8	A
5	3.2	T5-T6	A
6	4.3	C5-C6	A
7	1.7	T5-T6	A
8	3.7	T7	A
9	1.0	C3	A
10	6.2	C4-C5	A

Study Design

Testing took place over 7 sessions for each participant (Figure 1). The initial meeting consisted of obtaining informed consent and completing health history questionnaire. Experimental days one through five consisted of only completing questionnaires. Experimental day six involved completing an acute bout of home-based ESE as prescribed by the investigators in addition to completion of the questionnaires. Days one through five were used as a run-in period as to attempt to limit type 1 error due to novelty of questionnaires alone. This was done to ensure participants are in a stable condition and will provide a baseline for data comparison and subsequent analysis.

Figure 2

Study 1: Study Design



	Day 1	Days 2-5	Day 6			
	N/A	N/A	Upon Wake	1-Hour Prior	Post	Before Sleep
BAM	x	x	x	x	x	x
VAS-P	x	x	x	x	x	x
VAS-S	x	x	x	x	x	x
PANAS	x			x		x
PHQ-8	x			x		x
GAD-7	x			x		x
SCI-QLI	x			x		x

Study Procedures

During visit one, participants were required to read and sign an informed consent, followed by completing a medical and health history questionnaire. Next all participants were instructed on proper set-up and use of the electrical stimulation device (PowerDot, Carlsbad, California, USA) for knee extension and flexion exercise. In brief, the electrical stimulation device required two electrodes to be placed either over the inferomedial and inferolateral anterior thigh superior to the patella for knee extension or inferomedial and inferolateral posterior thigh just superior to the popliteal fossa for knee flexion and the third electrode placed superior to each set of electrodes respectively which served as a ground. During the ES exercise session, stimulation of the quadriceps for 24 minutes was completed first and then on the hamstrings for an additional 24 minutes. For their exercise sessions subjects utilized a pre-programmed ES protocol which consisted of 5 seconds of symmetrical biphasic stimulation at 40 Hz, with a 208 μsec pulse width for contractions and symmetrical biphasic pulse at 4 Hz for five seconds during recovery. The intensity, which was based on tolerance and visual feedback of an active muscle contraction, ramped up over the first 2 seconds and ramped down over the last 0.5 seconds of each 5 second stimulation period. This cycle of stimulation and recovery repeated for 24 minutes for each muscle group (48 minutes of total exercise).

Next, participants were instructed on how to properly complete the daily questionnaires on their personal use electronic devices via Qualtrics (Provo, Utah, USA). In brief, participants received an email link for all required time points which were mailed out at 5 a.m. each day and labeled explicitly for required time of completion. Participants were requested to complete the questionnaires at the same time each day. For quality control participants were asked to self-report if they did not complete a questionnaire or changed their typical time, which was

monitored by the research team through Qualtrics response system. In addition, participants were given autonomy when deciding when they will complete their ESE.

Experimental Sessions

On day one, participants will complete all questionnaires: BAM, PANAS, PHQ-8, GAD-7, SCI-QLI, VAS-Pain, VAS-Spasticity. On days two through five, participants only completed the BAM and the VAS for pain and spasticity. No exercise sessions were completed during these first five days. During experimental day six, immediately upon wake, subjects used their personal smart device to complete the BAM and VAS for pain and spasticity. Participants were then instructed to go about their typical day. One-hour prior to their scheduled exercise session participants completed the BAM, VAS, PHQ-8, PANAS, GAD-7, and SCI-QLI. The BAM and VAS were completed again immediately post exercise. Finally, the entire series of questionnaires were completed immediately before bed.

Questionnaires

See questionnaires utilized in study one below.

Brief Assessment of Mood (BAM)

The brief assessment of mood (BAM) is an abbreviated version of the Profile of Mood States (Searight & Montone, 2017). The BAM consists of six mood adjectives: angry, vigor, fatigued, depressed, confused, and tense (Dean et al., 1971). These six items are rated along a 5-point Likert scale with 1 standing for nothing at all and 5 signifying extremely, with participants responding how they feel in the moment at the time of completion. To calculate TMD, the Vigor score is subtracted from the sum of the five other mood items, with higher scores indicating higher TMD. The EI is assessed as a ratio of vigor to fatigue, with a higher score indicating a greater level of recovery. Importantly, the EI is more informative than Fatigue and Vigor scores alone as it

assesses the opposing effects of both constructs. Initial validation of the BAM TMD on college students (n = 621), BAMD TMD scores were highly correlated with profile of mood sates TMD scores (r = .88, $p < 0.001$) along with the Cronbach's coefficient alpha for the BAM TMD being acceptable (a = .75) (Dean et al., 1971). Lastly, EI has been shown to be correlated to changes in neuroendocrine response to the Ironman competition (Odagiri et al., 1996).

Visual Analog Scale Pain and Spasticity (VAS-P, VAS-S)

Pain and spasticity were assessed using a visual analog scale. A 10-cm line was anchored with "No Pain" or "No Spasticity" on the right and "Worst Pain" or "Very Frequent Spasticity" on the left for pain and spasticity, respectively. Pain and spasticity were then reported as the distance in cm from the left anchor to the point where the participant marked the line. Assessing pain and spasticity in this manner is a reliable and valid scale for participants over the ages of 18 (Bijur et al., 2001; Sköld, 2000).

Positive and Negative Affect Schedule (PANAS)

The positive and negative affect schedule is a self-reported assessment that consists of various words and synonyms that describe feelings and emotion (Magyar-Moe, 2009). The PANAS has been used as a self-reported measure in community and clinical contexts (Merz et al., 2013). The PANAS allows users to respond to 64 items utilizing a 5-point Liker scale with 1 signifying "slightly or not at all" up to 5 "extremely". Clinical and non-clinical investigations have shown PANAS to be a valid assessment (Merz et al., 2013). It has been stated that the PANAS assess both positive and negative emotions for users from week-to-week as they engage in their life (Magyar-Moe, 2009).

Personal Health Questionnaire Depression Scale (PHQ-8)

This questionnaire utilizes eight items to assess depressive qualities, originally designed for large clinical studies (Kroenke et al., 2009). The questionnaire asks the participant to assess how they feel over the past two weeks for each of the eight items. The participant answers on a 4-point Likert-scale with 0 signifying "not at all" and 3 signifying "nearly every day". The assessment and subsequent prevalence of depression is defined by a PHQ-8 score greater than or equal to 10 (Kroenke et al., 2009). It has been shown that the PHQ-8 can be successfully utilized to define current depression in the general population (Kroenke et al., 2009).

General Anxiety Disorder (GAD-7)

The GAD-7 was originally developed to allow a brief, self-reported scale to identify cases of general anxiety disorder (GAD). The GAD-7 requires the participant to answer 7 items pertaining to how they have felt over the last two weeks (Spitzer et al., 2006). Scoring of 5, 10, and 15 are cut-off points for mild, moderate, and severe anxiety, respectively. When the cut-off score of 10 is used, the GAD-7 has a 89% sensitivity to detects GAD (Spitzer et al., 2006). It has also been shown the GAD-7 is a valid tool for screening for GAD (Spitzer et al., 2006).

Spinal Cord Injury Quality of Life (SCI-QLI)

The SCI-QLI is a quality-of-life questionnaire specifically designed for individuals with spinal cord injury. Previous work was completed to develop a revised version, which includes 37 items in each of two sections: one assessing satisfaction with life aspects and the other assesses the importance of those aspects. Each of these questions are assessed with a six-point bar graph scale ranging from 1 (not at all satisfied/important) up to 6 (very satisfied/important) (May & Warren, 2002). The SCI-QLI has been shown to have clinical validity for a SCI population with Pearson correlations of $r = 0.99$ (Jain et al., 2007; May & Warren, 2002).

Statistical Analysis

Statistical analyses were performed using SPSS software (IBM Corporation, Amonk, NY, USA). The BAM and VAS-P and VAS-S were averaged on days two through five, 7 through 14, and 16 through 24 and analyzed as 3 individual timepoints. All other questionnaires were assessed individually at each time point in analysis. Therefore, the BAM, VAS-P, and VAS-S was analyzed at 16 timepoints while remaining data was analyzed at seven timepoints. All data will first be assessed for homogeneity with Levene's test. In the event of a significant Levene's test data was ran via a one-way analysis of variances (ANOVA) and significance was assessed via Welch Test. In event of a significant main effect, post-hoc analysis was ran via Games-Howell as equal variances is not assumed. If Levene's test fails to reach significance, data was assessed via univariate analysis of variance. In the event of a significant main effect, post hoc least significant differences pairwise comparisons were completed. Adherence was expressed as a percentage. This was assessed via simple average of individual adherence percentage as expressed by division of sessions completed by sessions prescribed (20). All data are expressed as mean ± standard deviation (SD).

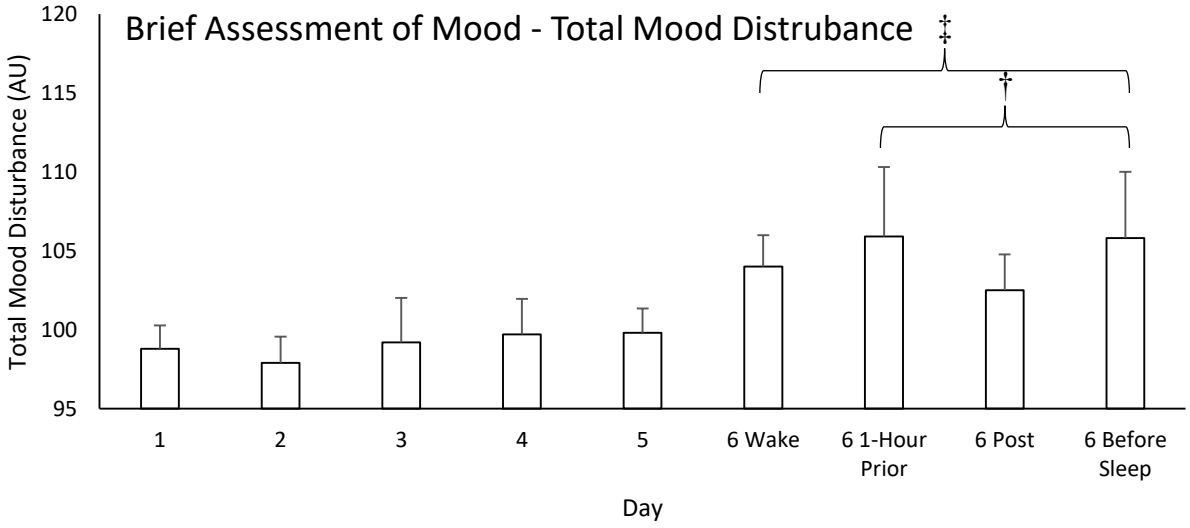
Results

Brief Assessment of Mood - Total Mood Disturbance

There was a main effect of day ($F = 12.7$, $p < 0.001$, $\eta^2 = 0.582$) for TMD (Figure 3). Participants TMD was increased compared to days one through five at Day 6 UW (all $p < 0.05$), Day 6 1H (all $p < 0.0001$), Day 6 IP ($p < 0.05$), and Day 6 BS (all $p < 0.0001$). Although, IP exercise was significantly lower than 1H and BS ($p = 0.015$).

Figure 3

Brief Assessment of Mood – Total Mood Disturbance

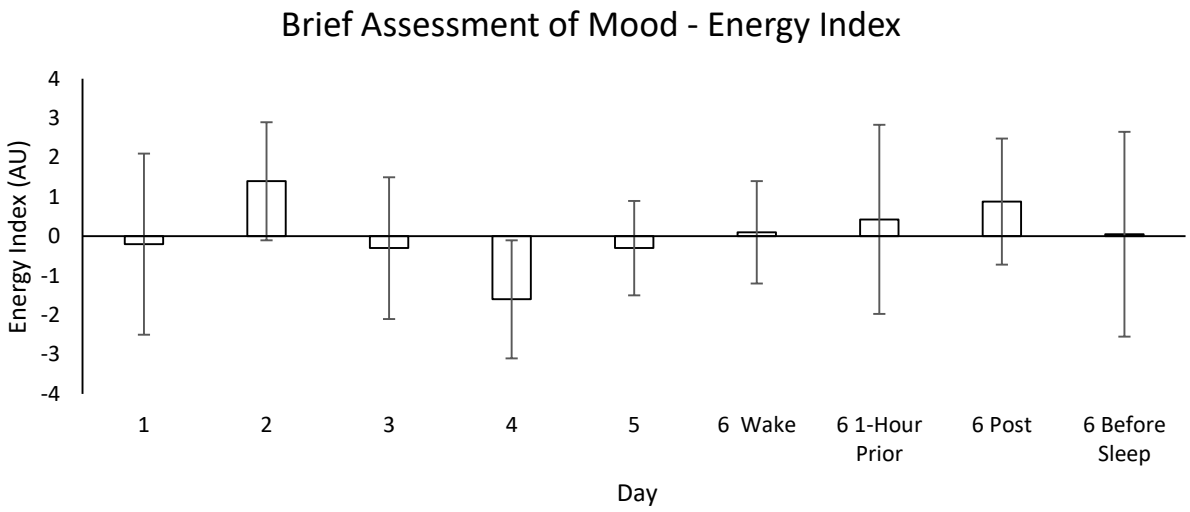


Brief Assessment of Mood - Energy Index

There was also a main effect of time for EI ($F = 2.1$, $p = 0.47$, $\eta^2 = 0.186$). Day four was significantly lower than Day two ($p < 0.0001$) (Figure 4).

Figure 4

Brief Assessment of Mood – Energy Index

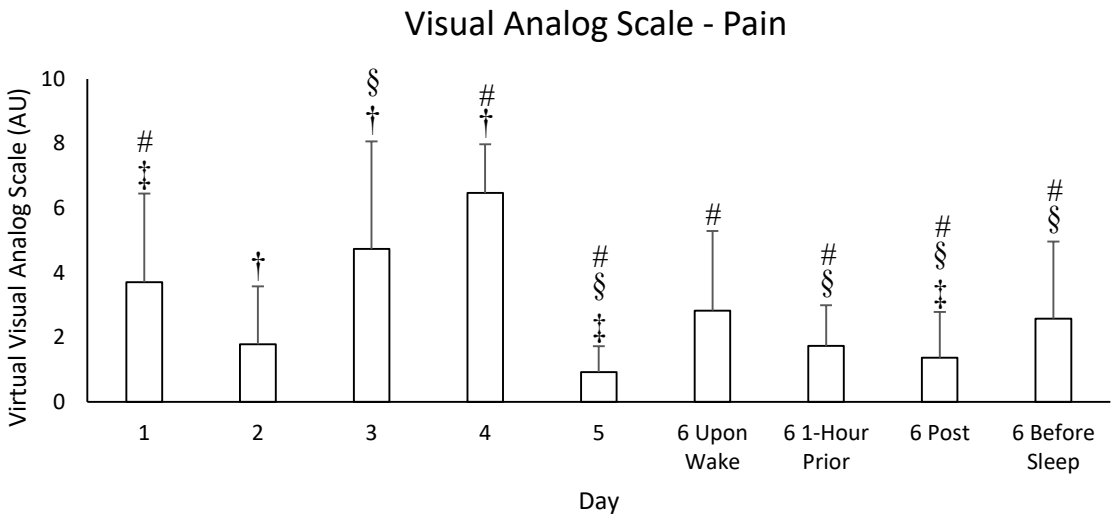


Self-reported Pain (VAS-P)

There was a main effect of day ($F = 6.3$, $p < 0.0001$, $\eta^2 = 0.437$) on pain based on the visual analog scale (Figure 5). Day five and IP was significantly lower than day one ($p = 0.005$, $p = 0.040$; respectively). Day two was significantly lower than day three and four ($p = 0.011$, $p < 0.0001$; respectively). Day three was significantly higher than day five, UW, 1H, and BS ($p < 0.0001$, $p = 0.007$, $p = 0.004$, $p = 0.036$; respectively). Day four was significantly higher than Day one, Day five, UW, 1H, IP, and BS ($p = 0.005$, $p < 0.0001$, $p = 0.001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$).

Figure 5.

Visual Analog Scale - Pain



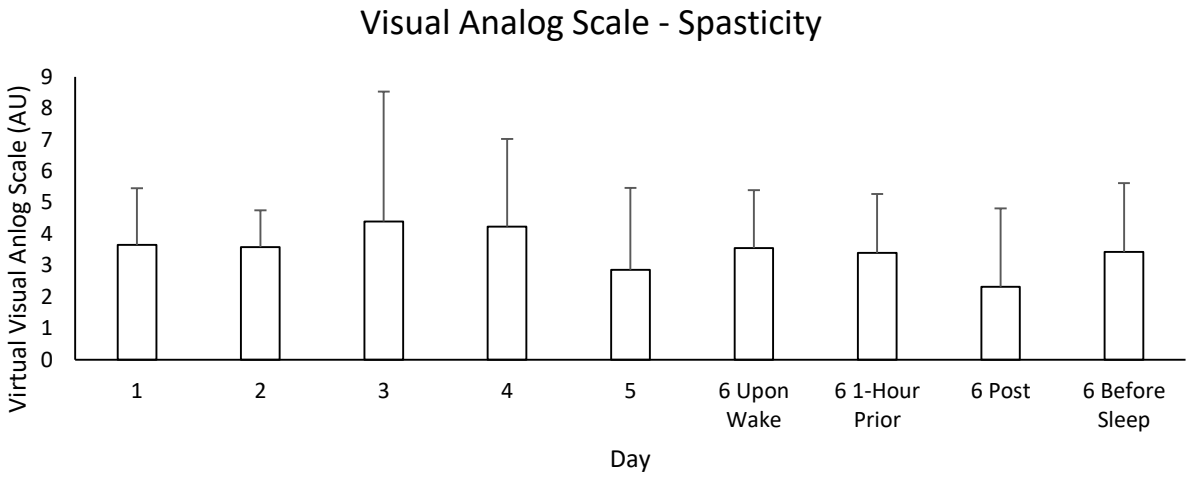
‡ Day one was higher compared to day five and day six post; † day two lower than day three and four; § day three higher than day five and day six upon wake, one-hour prior, and before sleep; # day four higher than day one, five, and day six upon wake, one-hour prior, post, and before sleep.

Self-reported Spasticity (VAS-S)

There was no main effect of day for spasticity ($F = 0.652$, $p = 0.732$, $\eta^2 = 0.063$) (Figure 6).

Figure 6

Visual Analog Scale - Spasticity

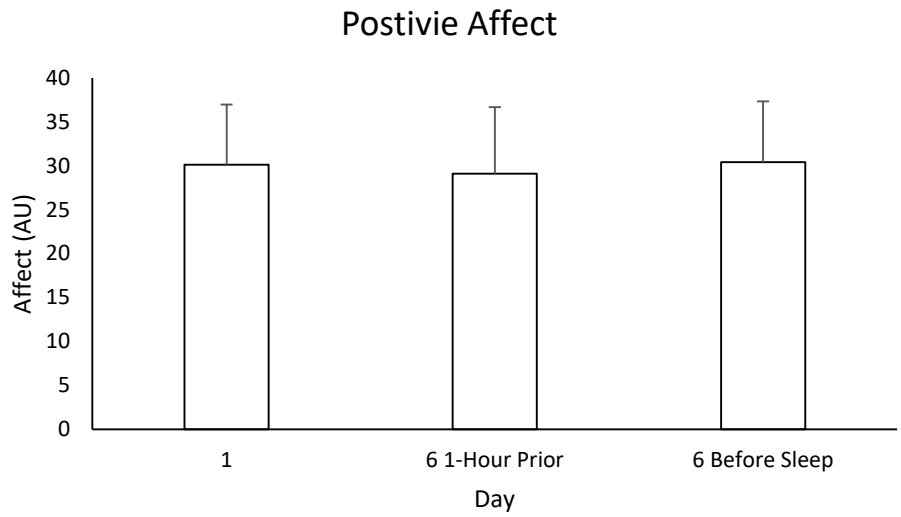


Positive Affect – (PANAS)

There was no main effect of day for positive affect ($F = 0.091$, $p = 0.913$, $\eta^2 = 0.007$) (Figure 7).

Figure 7

Positive and Negative Affect Schedule – Positive Affect

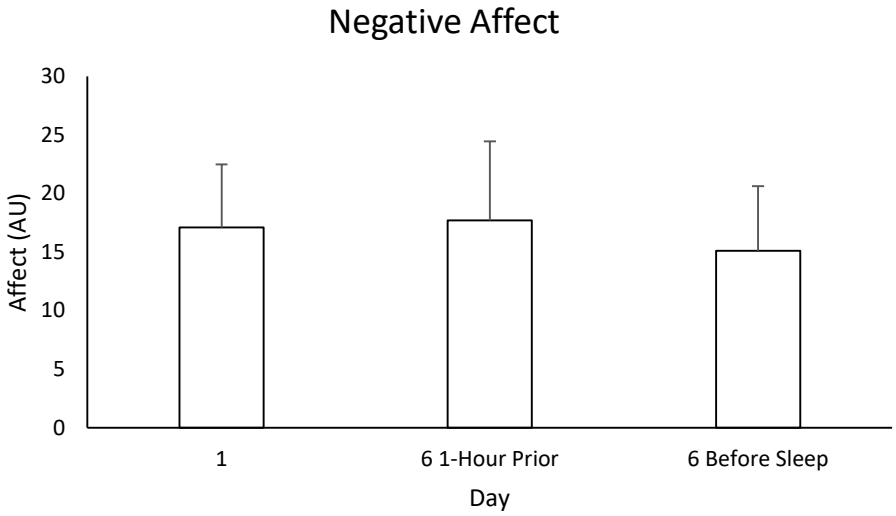


Negative Affect – (PANAS)

There was no main effect of day for negative affect ($F = 0.469$, $p = 0.631$, $\eta^2 = 0.036$) (Figure 8).

Figure 8

Positive and Negative Affect – Negative Affect

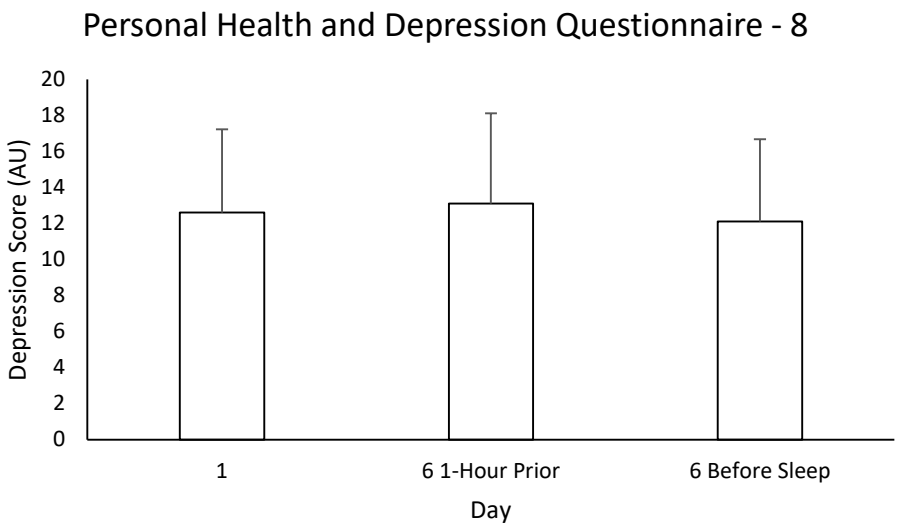


Depression (PHQ-8)

There was no main effect of day for depression scores ($F = 0.089$, $p = 0.915$, $\eta^2 = 0.008$) (Figure 9).

Figure 9

Personal Health and Depression Questionnaire - 8

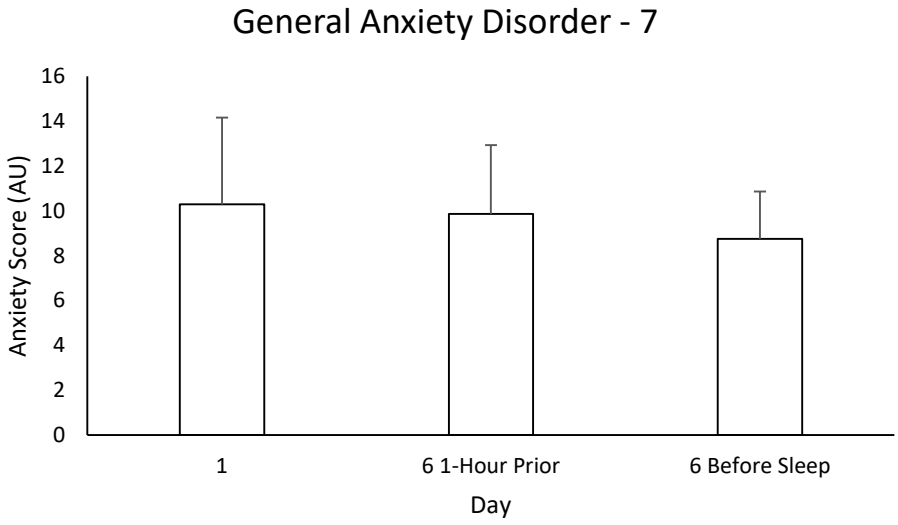


Anxiety (GAD-7)

There was no main effect of day for anxiety scores ($F = 0.543$, $p = 0.589$, $\eta^2 = 0.128$) (Figure 10).

Figure 10

General Anxiety Disorder - 7



Quality of Life (SCI-QLI)

Changes in quality of life over time are displayed in Figure 11. There was no main effect of day for quality-of-life scores ($F = 0.594$, $p = 0.559$, $\eta^2 = 0.129$).

Figure 11

Quality of Life – Spinal Cord Injury

Discussion

The purpose of this study was to assess the effects of a single home-based ESE session on various mood states in people with complete chronic SCI. The results failed to confirm our hypothesis that an acute bout of ESE would have benefits to TMD, EI, anxiety, pain, or spasticity. Moreover, data shows that upon the first day of exercise (day 6) TMD was higher at all time points. Although, there appeared to be a reduction in TMD immediately-post exercise when compared to one-hour prior and before sleep. Lastly, as hypothesized there was no acute effects of ESE on SCI-QLI, PANAS, and PHQ-8 questionnaires.

Interestingly, although TMD was elevated compared to the run-in period during with the addition of exercise, TMD was reduced immediately post exercise compared to one-hour prior and before sleep, indicating a transient reduction in mood disturbance. A recent investigation indicated that TMD in patients with incomplete SCI and multiple sclerosis (MS) was reduced immediately post and one-hour post, 30-minutes of cardiorespiratory exercise at 60% VO_{2Peak} (Donia et al., 2019). It should be noted exercise was completed using a Nu-Step which allows for ESE of the lower-limbs while the arms are volitionally involved, while the exercise in the current investigation only included lower limb ES. When assessed in abled-bodied individuals, it was shown that participating in exercise in bouts of 25 minutes to 60 minutes with recovery times of five minutes to 30minutes all reduced depression, hostility, and fatigue profile of mood states (Crush et al., 2018). Therefore, acute exercise appears to benefit TMD immediately post exercise, although the time course of these effects in this population remains unknown as TMD returned back to the same levels BS as seen at UW and 1HP to exercise.

Energy index did not appear to be positively affected from the acute addition of exercise. As previously stated it has been shown that acute aerobic exercise reduced TMD (Donia et al.,

2019). Interestingly, the previously mentioned study showed no effect on sub-constructs of vigor and fatigue, which EI is derived from (Donia et al., 2019). In abled-bodied individuals, aerobic cycling exercise improved vigor after one, three, and six weeks of exercise while fatigue was reduced after weeks three and six (Dishman et al., 2010). Therefore, the current study investigation agrees with previous literature that an acute bout of exercise does not have any affect upon EI in patients with SCI and MS but disagrees with abled-bodied studies.

The exercise session had no effect on spasticity which agrees with the current literature collated in a systematic review (Thomaz et al., 2019) that also indicates no effect of ES on spasticity. There was also no benefit of the current investigations exercise bout on VAS-P. This disagrees with current literature which has shown that ESE reduces pain as assessed with visual analog scale (Bi et al., 2015; Celik et al., 2013; Norrbrink, 2009). All previous studies only assessed pain via VAS after chronic interventions ranging from 10 days to 12 weeks, therefore an acute bout of ESE does not appear to be sufficient enough in reducing pain as assessed via VAS.

Exercise and positive and negative affect have a complex relationship. Exercise intensity, exercise duration, exercise dose (a product of frequency, intensity, and duration), and post-exercise assessment time have all been extensively investigated with regard to positive affect (Reed & Ones, 2006). It has been reported that walking had benefits on positive affect (Ekkekakis et al., 2005), while high intensity exercise resulted in negative responses (Pronk et al., 1995). Additionally, positive affect has been shown to peak at 5 minutes post exercise when assessed for trait (Ekkekakis et al., 2005; Petruzzello et al., 1997, 2001). The current investigation showed no effect on positive affect which may be due to PANAS assessing state affect, which would not show alterations in acute transient changes, which is a limitation to this

investigation. Additionally, the participants lacked sensory feedback and therefore viewed their time spent exercising as having low perceived return on the physical investment to exercise (Gorgey, 2014; Kehn & Kroll, 2009). Therefore, this data suggests that the addition of an acute bout of ESE does not modulate positive affect.

A recent report indicated reduced negative affect even with self-reported daily occurrence of stressors when individuals participated in exercise (Puterman et al., 2017), therefore indicating the ability of exercise to offset negative affect even in the presence of stressors. A recent study investigated the mitigating effects of exercise during the COVID-19 pandemic in college students in China. Their results indicated that to reduce negative affect individuals needed 108 minutes of light, 80 minutes of moderate, or 45 minutes of vigorous physical activity daily (Zhang et al., 2020). This volume of exercise is echoed in an investigation that reported reductions in negative affect over the course of 12-weeks where participants worked up to 150 minutes of moderate intensity aerobic exercise weekly (Abrantes et al., 2019). Therefore, the lack of change in negative affect in the current investigation is most likely due to the total volume (intensity and duration) of exercise in the current protocol. Additionally, this questionnaire investigated trait affect and therefore may have failed to adequately assess state shifts in response to exercise.

It is well known that individuals who participate in regular physical activity are less likely to have generalized anxiety disorder (Goodwin, 2003; Ströhle et al., 2007). Acute aerobic exercise has been reported to reduce anxiety immediately and up to 120 minutes post-exercise (Bahrke & Morgan, 1978; Hale & Raglin, 2002; Raglin & Wilson, 1996). The current investigation utilized a non-traditional form of knee extension and knee flexion exercise more similar to resistance exercise. Acute resistance exercise preformed at either 50-55% or 80-85%

1-repetition max resulted in immediate increases in anxiety with subsequent reductions at 20 and 40-minutes post-exercise (Bibeau et al., 2010). The current investigation found no change in anxiety when assessed at baseline, 1HP to exercise, and BS. Agreeing with the style of intervention used, it was shown that aerobic exercise but not resistance exercise had reduction in anxiety 60-minutes post-exercise (Garwin et al., 1997). The acute reduction in anxiety as shown in previous investigations may have been missed in the current study due to questionnaire assessing trait anxiety instead of state.

Physical activity, specifically aerobic exercise, has been shown to be an effective treatment and prevention of depression (Nyström et al., 2015; Schuch et al., 2018), the effects of an acute bout of resistance exercise are far less understood. A recent study of 23,635 German adults indicated that those who self-reported participation in resistance exercise at least once per week had reduced depression symptom severity (Bennie et al., 2020). Interestingly, a study assessed either 30-minutes of exercise at 60-70% age-predicted maximal heart rate versus or quiet rest and found that self-reported symptoms of depression were reduced in both conditions (Bartholomew et al., 2005). Therefore, while acute aerobic exercise may be sufficient to alter symptoms of depression, resistance exercise may require chronic adaptation to derive benefits. Again, it should be noted that these questionnaires were assessing trait characteristics and therefore may have failed to adequately discern acute changes in feelings of anxiety and depression.

Lastly, the current study's intervention failed to modulate the participants view on quality of life as hypothesized. It is well known that in individuals with SCI there is a strong correlation between physical activity level and quality of life (Stevens et al., 2008). Unfortunately, it remains to be elucidated on how constant the physical activity must occur for individuals to

perceive benefits in self-reported quality of life. As participants in the current investigation were asked to caseate exercise during the run-in period prior to their first day of exercise, it is likely the acute bout was not enough of a stimulus to derive a change in noticeable muscle quality change or quality-of-life perception.

Conclusions

Together, this investigation rejected our hypothesis that an acute bout of home-based ESE in patients with SCI would benefit energy index, pain, spasticity, and anxiety while confirming our hypothesis that the acute exercise would have no effect on positive and negative affect, depression or quality of life. A novel finding is that an acute bout of home-based ESE appears to have a transient effect on TMD immediately post-exercise even when mood is in a disturbed state. The length of this reduction in TMD after exercise remains uncertain as TMD was elevated again prior to sleep. The design of this study was unique in regard to exercise completion which was done by the participant in the confines of their home. Non-social home-based exercise may not be beneficial for this population, as it has been shown that social domains such as family and friends are a large predictor of self-reported quality-of-life (Tasiemski et al., 2005). Future studies need to investigate the time-course of exercise after a period of inactivity along with community-based setting to better understand the effects of ESE in this population along with questionnaires centered on state levels of function and feeling to better assess acute changes.

Funding

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Conflict of Interest

The authors declare no conflict of interest.

CHAPTER V

STUDY 2

Chronic effects of home-based electrical stimulation exercise on various mood states and quality of life.

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Introduction

Dependent upon injury location, spinal cord injury often results in permanent loss of muscle functionality (Eckert & Martin, 2017; Hachem et al., 2017). As of 2020, 17,810 new individuals each year sustain a spinal cord injury (*National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance*, 2019). Approximately 288,000 persons living with SCI in the United States, with 20.2% and 11.5% classified as either complete paraplegia or tetraplegia; respectively (*National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance*, 2019). While the physical effects of SCI are recognizable, psychological and emotional disturbances also occur. Depression has a prevalence of 11% to 30% in individuals with SCI (Brazeau & Davis, 2018; Craig et al., 1996; Hoffman et al., 2011). A cross-sectional investigation of 134 adults reported 49.3% exhibit mild to sever depression as defined by the Beck Depression Inverntory (Khazaeipour et al., 2015). This is of concern when compared to only 6.7% of abled bodied individuals reporting mild to severe depression (*2017 National Survey on Drug Use and Health: Methodological Summary and Definitions*, 2017). Anxiety also affects this population disproportionately with incidence of 19.3% vs. 14.1%; SCI and able-bodied, respectively (Peterson et al., 2020). Fortunately, non-pharmacological means exist for improving mood and quality of life.

As SCI incurs chronic disability, long-term quality of life becomes an important measure (McGee, 2001). A barrier for autonomy following SCI may result due to a reduction in physical fitness (Anneken et al., 2010; Noreau & Shephard, 1995). It has been shown that those who have SCI and participate in the most physical activity also report the greatest social support, which is also a strong indicator of quality of life (Kim et al., 2020). Individuals with SCI who participate in physical activity (PA) appear to have better quality of life in domains of physical,

psychological and social contexts compared to those who do not participate in PA (Anneken et al., 2010; Tasiemski et al., 2000). The benefits due in part by regular exercise include reduction in stress and tiredness and increases in mood, energy, stamina, and mental alertness have been promoted for nearly all populations (Sharma et al., 2006). Furthermore, those with SCI who participate in exercise have improved scores in depression screening (Kim et al., 2020) as well as reductions in pain and fatigue (Tawashy et al., 2009). The reduction in pain is important as pain has a significant impact on long-term exercise adherence in the SCI population (Dolbow et al., 2012). .

Barriers to exercise exist including perceived low return on physical investment, lack of accessible facilities, transportation, and fear of injury (Gorgey, 2014; Kehn & Kroll, 2009) all of which contribute to reduce participation and adherence to exercise program in the SCI population (Scelza et al., 2005). Interestingly, it has been reported that adherence to a home-based electrical stimulation cycling exercise program in the SCI population is 71.7% compared to the average exercise adherence of the general population of 31% (Dolbow et al., 2012). Furthermore, electrical stimulated exercise (ESE) has been utilized to help improve over-all health and QOL for individuals with complete SCI and other disabilities (Allison et al., 2016; Bauman et al., 2016; Bélanger et al., 2000; Bersch et al., 2015; Bochkezanian et al., 2018; Burke et al., 2016; Coquart et al., 2016; Crevenna et al., 2006; Helmkamp, 1995; Kern et al., 2014; Natsume et al., 2015). With the advent of the COVID-19 pandemic and orientation to stay at home, there is a necessity to deliver exercise to the home environment. ESE allows the innervation of lower limb musculature, which are typically otherwise sedentary in patients with complete SCI. although there are reports that ESE improves depression, mental health and QOL in individuals with heart failure (Karavidas et al., 2006), cancer (Crevenna et al., 2006) and

chronic back pain (Durmus et al., 2009) there is a paucity of knowledge on the effect of home based ESE on QOL and depression in those with SCI.

Therefore, the aim of this investigation is to assess feasibility of adherence and chronic effects of a four-week home-based ESE program and the acute effects on feelings of anxiety, depression, quality of life, pain, and spasticity. We hypothesize that four-weeks of home-based ES will have positive effect on total mood disturbance and energy intake via the brief assessment of mood (BAM) questionnaire, anxiety via the general anxiety disorder (GAD-7), pain and spasticity assessed via visual analog scale (VAS), positive and negative affect (PANAS), personal health questionnaire depression scale (PHQ-8) and spinal cord injury quality of Life 23 (SCIQL-23). Additionally, we hypothesize that participants will maintain an exercise adherence similar to what is typically observed in other clinical populations of 80% (Bullard et al., 2019).

Materials and Methods

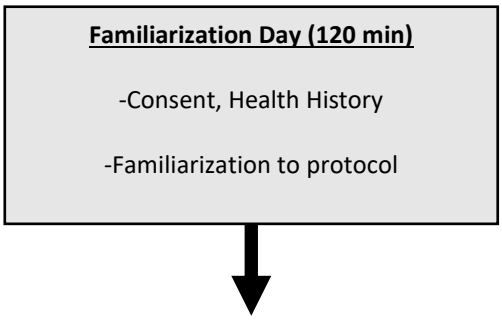
Twelve individuals with complete spinal cord injury were recruited. A priori sample size estimation was conducted according to Beck (2013) and mentioned previously. Two individuals were excluded due to personal medical reasons. Therefore, a total of 10 participants were included in the analysis. Inclusion criteria Participants were post-injury by at least 1 year (average 5.2 ± 9.2 years) post-injury and between 20-54 years of age. Descriptive characteristics about participants can be found in Table 1. Exclusion for participation in the study includes evidence of lower motor neuron injury, internal pacemaker or defibrillator, active infection or disease, history of autonomic dysreflexia, unable to speak English, no access to smart device or reliable internet connection, and severe reaction to electrode adhesive. All participants had a history of using ES. All participants that were currently participating in ESE (n = 3) ceased activity for one week prior to the study and for the duration of the study. Participants that were completing non-ESE were informed to continue to complete their routine exercises (n = 9). The research protocol and the informed consent were approved by the University's Institutional Review Board.

Study Design

Testing took place over 26 sessions for each participant (Figure 12). All required equipment was either mailed or delivered to the participants. Session one consisted of providing informed consent, written consent and medical and health history. Experimental days one through five consisted of only completing questionnaires. Days one through five were used as a run-in period as to attempt to limit type 1 error. This allowed for researchers to obtain a baseline for each individual prior to the addition of the ESE program so participants could serve as their own controls. Day six marked the first day of a 20 session home based ESE program. Exercise sessions were required to be completed each day Monday through Friday for a total of five ESE session per week. Experimental days 6, 15, and 25 consisted of ESE and four sets of questionnaires throughout the day.

Figure 12

Study 2: Study Design



	Day 1	Days 2-5	Day 15				Days 7-14	Day 15				Days 16-24	Day 25			
	Volitional	Volitional	Upon Wake	1-Hour Prior	Post	Before Sleep	Before Sleep	Upon Wake	1-Hour Prior	Post	Before Sleep	Upon Wake	Upon Wake	1-Hour Prior	Post	Before Sleep
BAM	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
VAS-P	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
VAS-S	x	X	x	x	x	x	X	x	x	x	x	x	x	x	x	x
PANAS	x			x		x			x		x			x		x
PHQ-8	x			x		x			x		x			x		x
GAD-7	x			x		x			x		x			x		x
SCI-QLI	x			x		x			x		x			x		x

Study Procedures

During initial patient contact, participants were required to read and sign an informed consent, followed by completing a medical and health history questionnaire. Next all participants were instructed on proper set-up and use of the electrical stimulation device (PowerDot, Carlsbad, California, USA). In brief, the electrical stimulation device requires two electrodes to be placed either over the inferomedial and inferolateral anterior thigh superior to the patella for knee extension or inferomedial and inferolateral posterior thigh just superior to the popliteal fossa for knee flexion. A third electrode placed superior to each set of electrodes respectively as per manufacturers recommendation which served as a ground. During the ES exercise session, stimulation of the quadriceps for 24 minutes was completed first and then on the hamstrings for an additional 24 minutes. For their exercise sessions subjects utilized a pre-programmed ES protocol which consisted of 5 seconds of symmetrical biphasic stimulation at 40 Hz, with a 208 μsec pulse width for contractions followed by symmetrical biphasic pulse of 4 Hz, five seconds long for rest. This cycle of stimulation and rest repeated for 24 minutes for each muscle group (48 minutes of total exercise). The intensity, which was based on tolerance and visual feedback of an active muscle contraction, ramped up over the first 2 seconds and ramped down over the last 0.5 seconds of each 5 second stimulation period. As this was a home-based exercise program, and adherence is a dependent variable, there was no control set in place for completion time of prescribed exercise program.

Next participants were instructed on how to properly complete the daily questionnaires (described below) on their personal use electronic devices via Qualtrics (Povo, Utah, USA). In brief, participants received an email link for all required time points which were mailed out at 5 a.m. each day and labeled explicitly for required time of completion. Participants scheduled with

the investigator an approximate time they would complete daily exercise training which subsequently influenced when they would complete the questionnaires.

Experimental Days

On experimental day one, participants completed all questionnaires (BAM, PANAS, PHQ-8, GAD-7, SCI-QLI, VAS-Pain, VAS-Spasticity). On days two through five, participants will only complete the BAM and the VAS for pain and spasticity. No exercise sessions were completed during these first five days. On the sixth experimental day (which always began on a Monday) participants completed four sets of questionnaires. Upon wake (UW) and immediately post-exercise (IP), participants completed the BAM and VAS for pain and spasticity. One-hour prior (1H) to ESE and before sleep (BS), participants completed the BAM, PANAS, PHQ-8, GAD-7, SCI-QLI, and VAS for pain and spasticity. Experimental days 15 and 25 were identical to experimental day six. Conversely, experimental days 7-14 and 16-24 participants only completed ESE at the previously determined timepoint and the BAM and VAS for pain and spasticity. For completion for quality control Participants were asked to self-report if they did not complete a questionnaire or changed their typical time. This was monitored by the research team through Qualtrics response system.

Questionnaires

All questionnaires are previously described in detail (chapter 4)

Statistical analysis

Statistical analyses were performed using SPSS software (IBM Corporation, Amonk, NY, USA). The BAM and VAS-P and VAS-S were averaged on days two through five, 7 through 14, and 16 through 24 and analyzed as 3 individual timepoints. All other questionnaires were assessed individually at each time point in analysis. Therefore, the BAM,

VAS-P, and VAS-S was analyzed at 16 timepoints while remaining data was analyzed at seven timepoints. All data will first be assessed for homogeneity with Levene's test. In the event of a significant Levene's test data will be ran via a one-way analysis of variances (ANOVA) and significance will be assessed via Welch Test. In event of a significant main effect, post-hoc analysis will be done via Games-Howell as equal variances is not assumed. If Levene's test fails to reach significance, data will be assessed via univariate analysis of variance. In the event of a significant main effect, post hoc least significant differences pairwise comparisons were completed. Adherence was expressed as a percentage. This was assessed via simple average of individual adherence percentage as expressed by division of sessions completed by sessions prescribed (20). All data are expressed as mean ± standard deviation (SD).

Results

Exercise Adherence

Exercise adherence across four weeks of five times per week home-based

Table 2

Exercise Adherence

Participant 1	85%
Participant 2	100%
Participant 3	100%
Participant 4	100%
Participant 5	80%
Participant 6	100%
Participant 7	100%
Participant 8	100%
Participant 9	90%

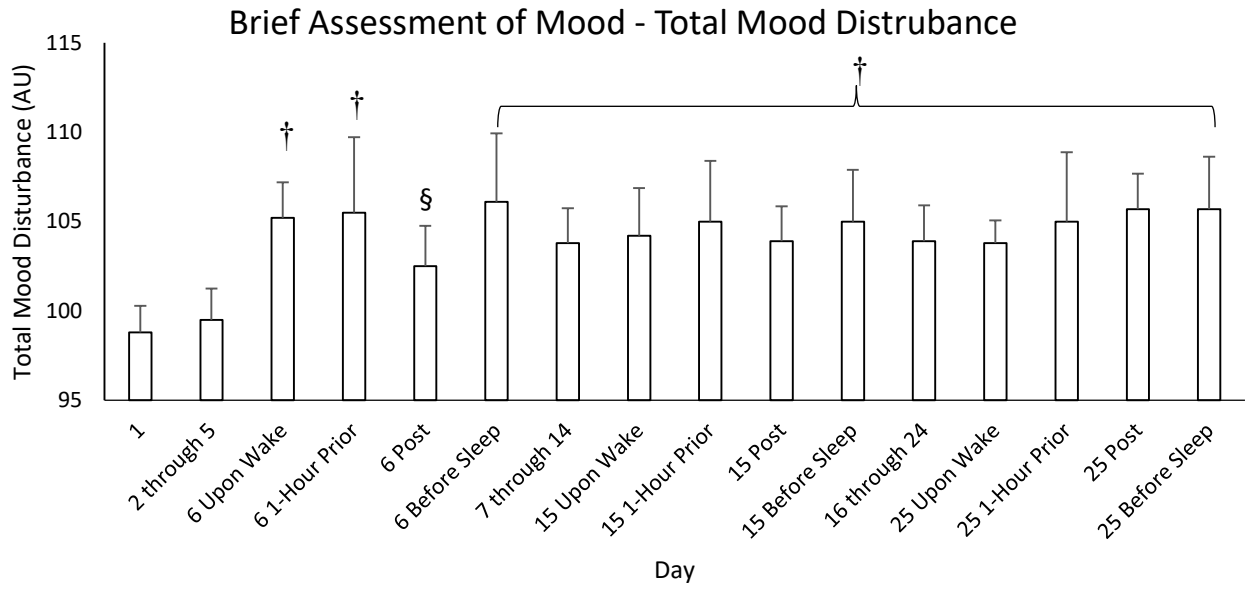
Participant 10	100%
Exercise Adherence	95%

Mood (BAM – TMD)

There was a main effect of day ((F_{Welch} (15, 41.2) = 9.70, $p > 0.0001$) for TMD (Figure 13). TMD was increased on all days (at least $p = 0.05$) than all other days besides day six IP and day one ($p = 0.071$, $p = 0.078$; respectively). Additionally, day six IP was lower than day six 1H ($p = 0.015$) and BS ($p = 0.015$).

Figure 13

Brief Assessment of Mood – Total Mood Disturbance



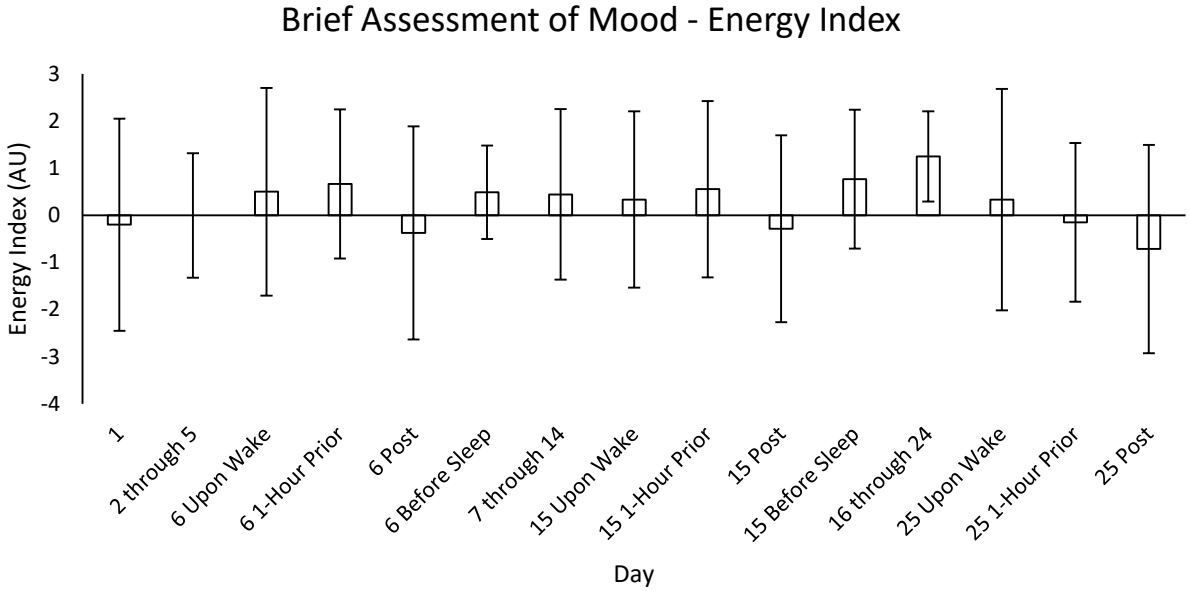
† Significantly different from days one and two through five; § significantly different from day six one-hour prior and day 6 before sleep.

Energy (BAM – EI)

There was no main effect for EI ($F = 0.548$, $p = 0.888$, $\eta^2 = 0.067$) (Figure 14).

Figure 14

Brief Assessment of Mood – Energy Index

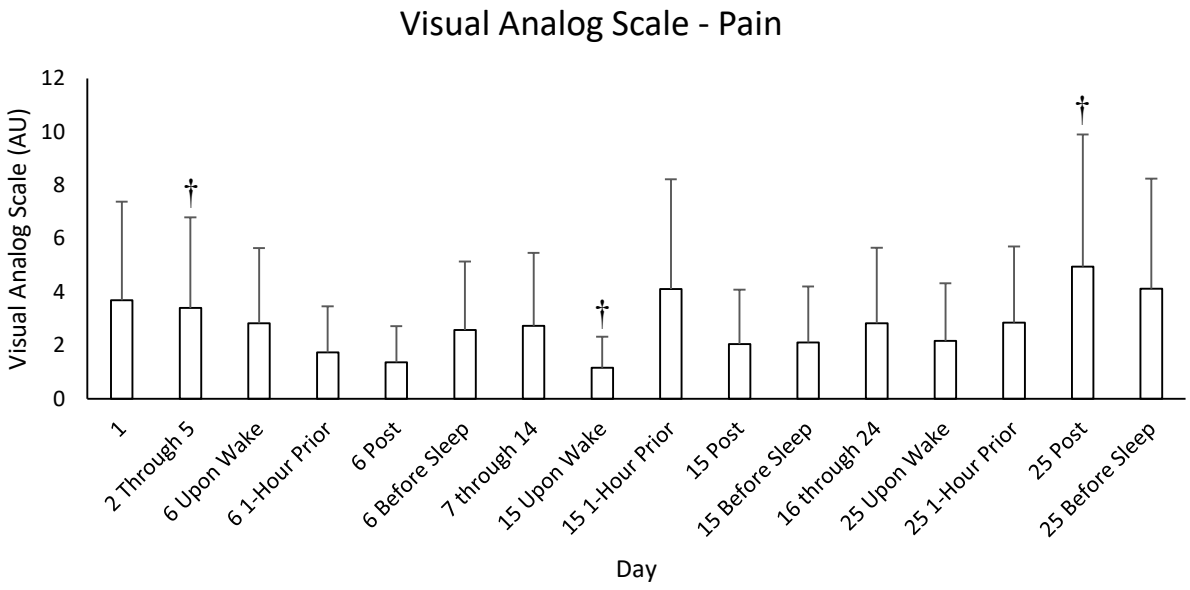


Pain (VAS-P)

There was a main effect of day for pain ((F_{Welch} (15, 30.9) = 10.3, $p > 0.0001$) (Figure 15). Day 15 upon wake was significantly lower days two through five and day 25 IP ($p = 0.001$).

Figure 15

Visual Analog Scale - Pain



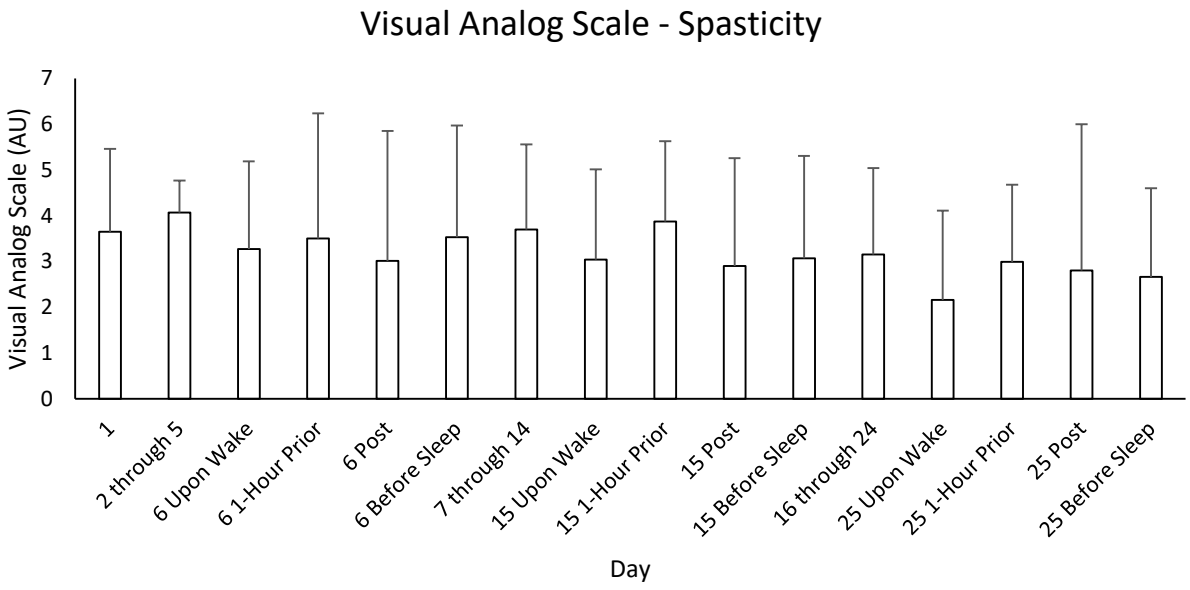
† Day 11 upon wake significantly lower than days two through five and day 25 post.

Visual Analog Scale - Spasticity

There was no main effect of day for spasticity (F = 0.258, p = 0.995, η^2 = 0.038) (figure 16).

Figure 16

Visual Analog Scale – Spasticity

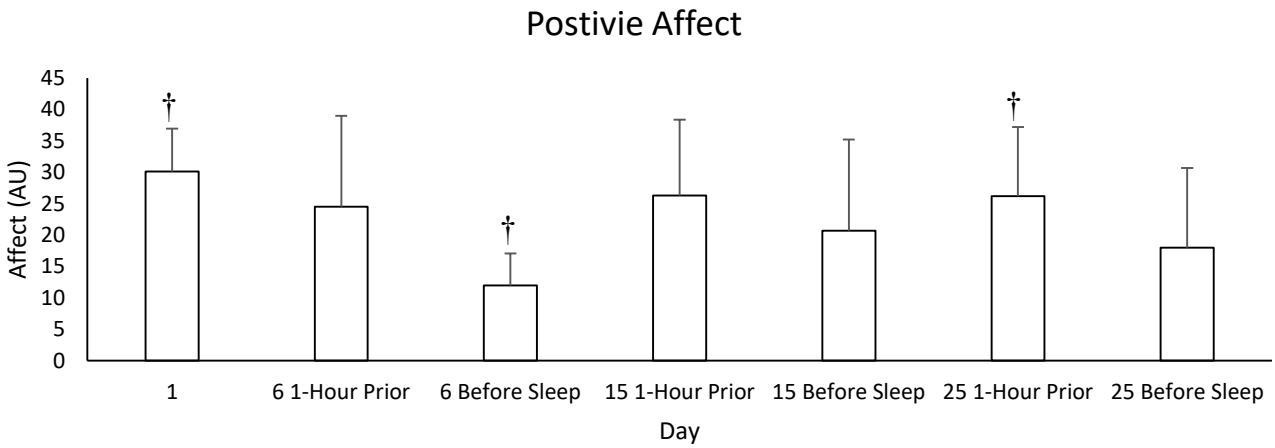


Positive Affect (PANAS)

There was a main effect of day for PANAS-POS ((F_{Welch} (6, 26.7) = 7.96, $p < 0.0001$) (Figure 17). Day six 1H was significantly lower than day one, and day 20 1H to exercise ($p < 0.0001$ and $p = 0.033$; respectively).

Figure 17

Positive and Negative Affect – Positive Affect



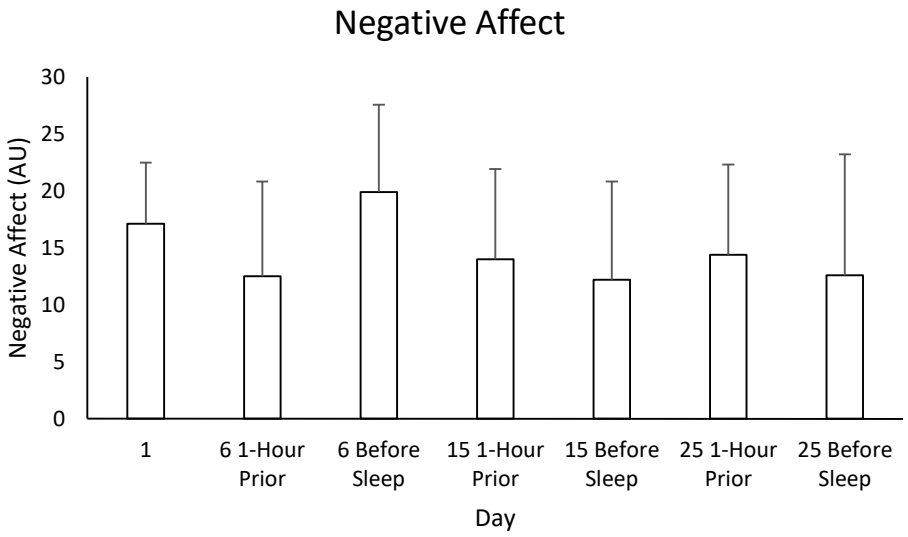
† Day 6 before sleep significantly lower than day one and day 25 one-hour prior

Negative Affect (PANAS)

There was no main effect of day for PANAS-Neg ($F = 1.2$, $p = 0.318$, $\eta^2 = 0.104$) (Figure 28)

Figure 18

Positive and Negative Affect – Negative Affect

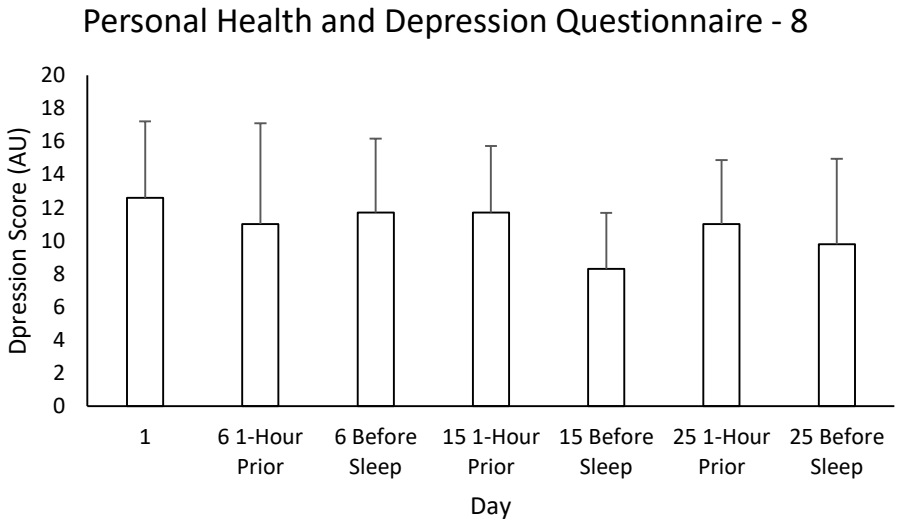


Depression (PHQ-8)

There was no main effect of day for PHQ-8 ($F = 0.869$, $p = 0.524$, $\eta^2 = 0.084$) (Figure 19).

Figure 19

Personal Health and Depression Questionnaire - 8

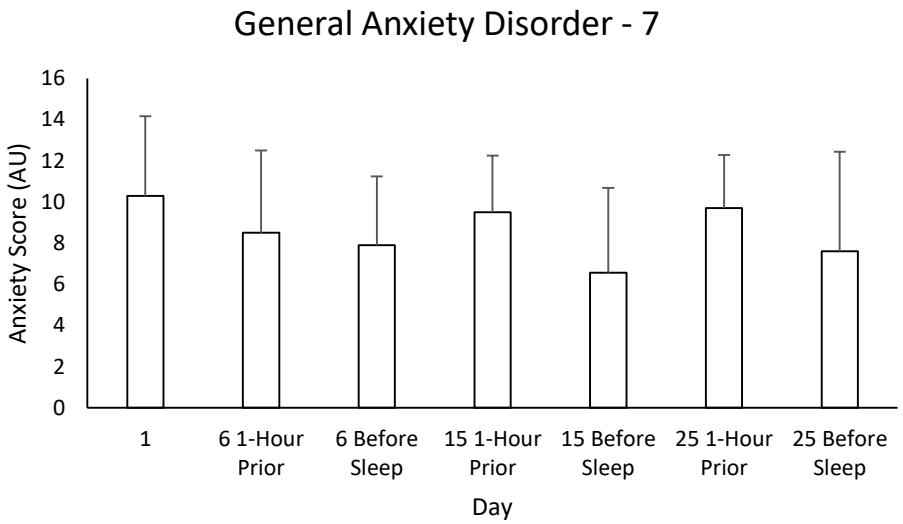


Anxiety (GAD-7)

There was no main effect of day for GAD-7 (F = 0.1.23, p = 0.304, η^2 = 0.106) (Figure 20).

Figure 20

General Anxiety Disorder - 7

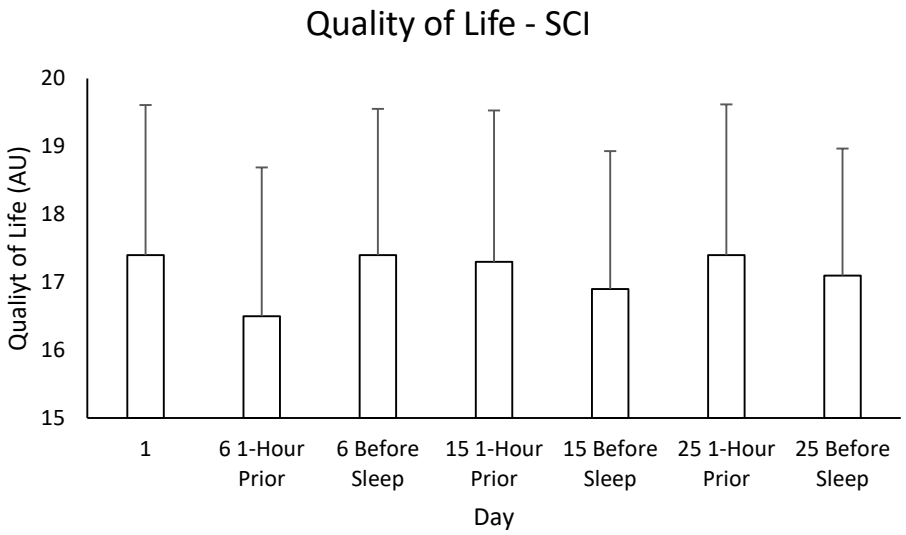


Quality of life (SCI-QLI)

Changes in self-reported quality of life over time are displayed in Figure 21. There was no main effect of day for SCI-QLI ($F = 0.156$, $p = 0.987$, $\eta^2 = 0.016$).

Figure 21

Quality of Life – Spinal Cord Injury

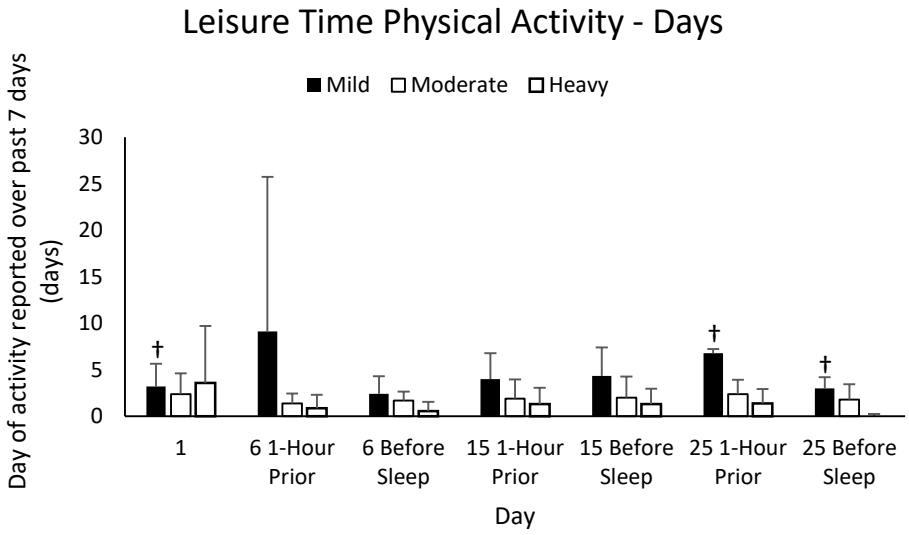


Leisure time physical activity days (LTPAQ-SCI)

There was a main effect of day for mild day (F_{Welch} (6, 17.4) = 11.0, $p < 0.0001$) (Figure 22). Reported mild days of exercise was significantly higher on day 25 1H compared to day one ($p = 0.013$) and day 25 BS ($p = 0.010$).

Figure 22

Long-term Physical Activity Questionnaire - Days



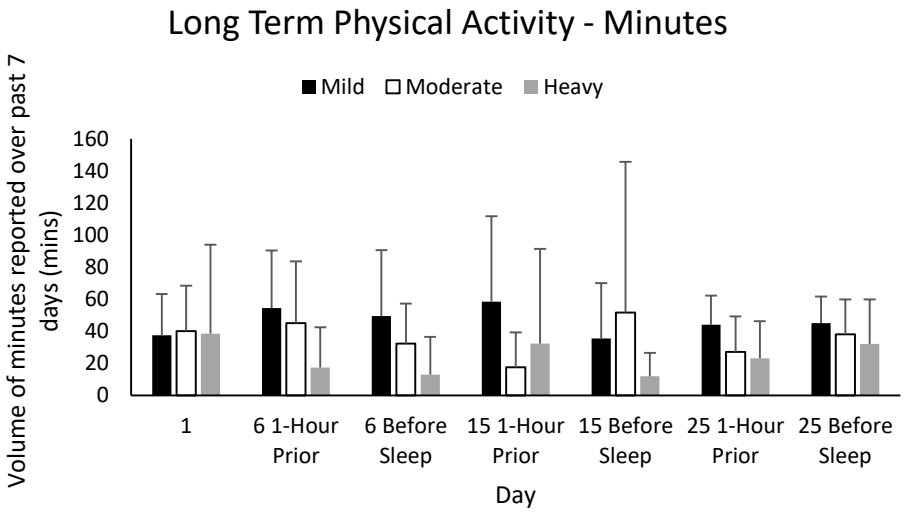
† Significantly higher than day one and day 25 before sleep

Leisure Time physical activity minutes (LTPAQ-SCI)

There was no main effect of day for mild minutes ($F = 0.434$, $p = 0.852$, $\eta^2 = 0.057$), moderate day ($F_{Welch}(6, 16.9) = 0.403$, $p = 0.867$), moderate minutes ($F = 0.161$, $p = 0.986$, $\eta^2 = 0.022$), heavy day ($F = 1.02$, $p = 0.419$, $\eta^2 = 0.116$), or heavy minutes ($F = 0.382$, $p = 0.887$, $\eta^2 = 0.051$) for self-reported physical activity parameters (Figure 23).

Figure 23

Long-term Physical Activity Questionnaire - Minutes



Discussion

The purpose of this study was to assess the chronic effects of a home-based ESE plan for people with complete chronic SCI. The current investigation failed to confirm our hypothesis that four weeks of home-based ESE exercise would benefit areas of mood, quality of life, pain, spasticity, and perception of physical activity participation. Specifically, data suggests there was no beneficial effect on mood disturbance, energy index, anxiety, depression, quality of life, negative affect, or physical activity for moderate and heavy days nor mild, moderate, or heavy minutes of exercise. Although, data reported indicates a main effect of day for self-reported mild days of exercise and positive affect, although this data should be interpreted with caution.

Utilizing the BAM, this investigation was able to assess transient changes in mood over time through daily assessment. Interestingly, our data indicates that with the addition of the ESE, TMD was actually raised when compared to the run-in week which included questionnaire completion only. Although, with the increase in TMD, day six IP exercise was lower than day six 1H and BS. A study utilizing abled-bodied participants cycling at either 75% or 40% VO_{2Max} for 20-minutes resulted in a reduction in TMD 10-minutes post-exercise after one, three, and six weeks of exercise three times weekly (Dishman et al., 2010). Moreover, an investigation utilizing incomplete SCI and multiple sclerosis participants completing 60% VO_{2Peak} exercise via Nu-Step, which resembles a recumbent elliptical exercise machine, had reduction in TMD immediately post-exercise and one-hour post-exercise compared to baseline (Donia et al., 2019). Additionally, there was no effect on vigor or fatigue (Donia et al., 2019), subconstructs that EI is derived from, agreeing with the current findings of this investigation that ESE does not benefit EI. The previously mentioned investigations share two important characteristics. Their participants had some form of sensory feedback along with partial volition of upper-body

movement, which was completely lacking in the current investigation's participants, which may influence perception of exercise completed. Secondly, the current investigation required participants to don and doff exercise equipment themselves and did not control for post-exercise questionnaire completion. Therefore, the effort of donning and doffing the device, lack of sensory feedback to activity, and overall utilization of small muscle mass during exercise may have caused the lack of beneficial change of TMD seen in the current investigation.

Individuals who participate in regular physical activity have been shown to be less likely to display generalized anxiety disorder (Goodwin, 2003; Jayakody et al., 2014; Ströhle, 2008) and has been known to reduce symptoms of depression (Cooney et al., 2013). A recent investigation assessed the relationship between anxiety and depression in individuals with spinal cord injury (Kim et al., 2020). The investigation data suggests that those in the highest level of physical activity (670.9 ± 354.9 minutes per week across mild, moderate, and strenuous intensities) had reduced self-reported anxiety (via the GAD-7) and depression (via the PHQ-9) when compared to the lowest physically active group (44.1 ± 52.7 minutes per week) (Kim et al., 2020). The current investigation did result in an increase in self-reported mild-physically active days on the last day of exercise, while self-reported physical activity minutes did not change and had a study wide average of 46.8 ± 34.7 mild, 42.9 ± 67.7 moderate, and 40.1 ± 88.3 heavy minutes of exercise. Therefore, it is likely that the current investigation failed to reach a sufficient volume and intensity of exercise for participants to derive benefits to either anxiety or depression. Interestingly, two other investigations reporting the benefits of exercise for patients with SCI on anxiety and depression specifically assessed individuals completing exercise in a social setting (i.e. team sports) (Gioia et al., 2006; Muraki et al., 2000). Comparatively, the current investigation participants exercised at home alone due to the COVID-19 stay at home

order. Therefore, there may also be underlying mechanisms of social support that additionally help with perception of exercise participation and subsequent benefits derived.

Positive and negative affect have been shown to be responsive to exercise intensity, exercise duration, exercise dose, and post-exercise assessment time (Reed & Ones, 2006). The current investigation resulted in no change in negative affect over the course of the exercise protocol. A recent investigation assessed the effect of 30-minutes of cycling at 65-75% of age-predicted maximal heart rate and found no significant difference in either positive or negative affect compared to quiet rest controls (Kyral et al., 2019). This study agrees with the current investigation for negative affect, although for positive affect there was a main effect of time where positive affect was higher on the first day of exercise one-hour prior compared to baseline and day 20 of exercise one-hour prior. It is challenging to interpret these results, but both positive affect and self-reported mild days of exercise were increased at day 20 one-hour prior. Therefore, the effect of more habitual exercise which has been shown to positively mediate affect (Pasco et al., 2011) may be the driving factor for this investigations results.

Of potential utmost importance is the adherence rate noted in this current investigation. In total 95% of all 200 exercise sessions across 10 participants were completed. This adherence supersedes that of other investigations mobile health investigations noting “high” adherence of 74% (Walter et al., 1999). Mobile health is an emerging and potentially impactful field of research to help special populations with chronic disease or those facing community mobility barriers. Recent work has shown that mobile health can result in clinically significant reductions in depression symptoms (Kryger et al., 2019) while helping to promote light to moderate physical activity in wheelchair users with SCI (Hiremath et al., 2019). Interestingly, an investigation utilizing home-based exercise videos for those with SCI reported less than half the

participants completed less tan 20% of the exercise videos (Wilroy et al., 2021). Therefore, this style of home-based intervention may house benefits in ensuring completion and adherence to maximize positive outcomes.

Conclusions

Collectively this investigation rejected our hypothesis that engaging in four weeks of home-based ESE exercise would benefits areas of mood, depression, anxiety, quality of life, and physical activity. An important finding was the very high (95%) adherence to exercise bouts over the four-week intervention. Therefore, use of equipment that mimic the style of intervention delivered by the PowerDot™ may help to ensure participant involvement and completion. A novelty of this investigation, to the authors knowledge, is the first investigation to assess the effects of home-based ESE with the orientation of stay at home due to COVID-19. Because of that, is it likely that many of the participants in this investigation were spending a majority if not all of their waking hours at home with greatly reduced social interaction. Social interaction has shown to be an important factor in quality of life, exercise adherence, and physical functioning (Anson et al., 1993; Müller et al., 2012; Post et al., 1999; van Leeuwen et al., 2010). Conversely, all other discussed studies involved participants to report to a research laboratory which all required a degree of social interaction, potentially with researchers that were appreciative of their involvement creating a supportive environment. The idea of group exercise as well as team-based sports have shown benefit in improving participation in exercise participation across moderate and strenuous intensities and quality of life (Crane et al., 2017). An investigation of self-reported physical activity in individuals with SCI concluded those participating in the highest volume of physical activity also had increased social support and reduced depression and anxiety scores when compared to those moderately and mildly active confirming the importance

of social support as an influence of physical activity (Kim et al., 2020). Importantly, this investigation assessed changes in trait characteristics compared to state which was utilized in the other investigations. Therefore, future investigations should assess trait and state levels of mental health to better understand small acute changes across time in additions to chronic effects.

Funding

This work was not supported by any external funding.

Conflict of Interest

The authors declare no conflict of interest.

APPENDICES

APPENDIX A.

INFORMED CONSENT

Informed Consent to Participate in a Research Study

Study Title: The effect of home-based electrical stimulation exercise on depression, anxiety and quality of life in those with SCI.

Principal Investigator: John McDaniel, PhD
Exercise Physiology
Kent State University

Co-Investigator: Cody Dulaney, ABD

You are being invited to participate in a research study. This consent form will provide you with information on the research project, what you will need to do, and the associated risks and benefits of the research. Your participation is voluntary. Please read this form carefully. It is important that you ask questions and fully understand the research in order to make an informed decision. You will receive a copy of this document to take with you.

Purpose: To assess the effect of at home electrical stimulation exercise on aspects of emotion and quality of life.

Procedures: The initial meeting will be set up either in person or over the phone to discuss the details of the research study and review this consent form. If the initial visit is in person, and you agree to participate, you will be given a health history questionnaire to complete and a PowerDot Smart Muscle Stimulator system. The investigators will provide you with complete instruction on how to use it. If the initial meeting is over the phone, an in-person meeting will be scheduled to collect the consent form and provide you the PowerDot system as well as the instructions for the device. The PowerDot system is a commercially available battery powered Neuromuscular Electrical Stimulation device that requires you to place 3 sticky electrodes on your skin over the target muscles (skin should be clean prior to use). There are pre-programed stimulation protocols on the device that we will prescribe to you. You will be able to adjust the intensity of the stimulation (through an application on your smart phone). During the instruction process we will determine what is the best stimulation intensity for you based on how your muscles respond. We will ask you to keep stimulation intensity no greater than 50% and we will provide you with an information sheet to with instructions to help maintain durability of the pads. We will also provide you with ankle weights if needed.

First 5 days- During the first 5 days you will not use the PowerDot system, rather we will ask you to complete a series of 5 questionnaires that focus on mood, depression, anxiety and quality of life, physical activity, pain and spasticity. The first day you will complete all questionnaires while on the remaining 4

days you will just complete one of them. This first 5 days is to simply establish a baseline. Together all questionnaires should take approximately 15-20 minutes to complete. The single questionnaire that you will repeat the most throughout this study will take less than one minute.

Testing day 1- On the 6th day you will be asked to complete all the questionnaires again several times throughout the day. This will take place before and after your training session. To begin the exercise session, you will place 3 stimulating electrodes (sticky patches) over the thigh on each leg as demonstrated during the initial meeting. Prior to continuing, you must document the time, date, and pad used on the record sheet provided. You will then begin a predetermined stimulation protocol. The stimulation and protocol parameters will be based on the PowerDot's recommended "prevention of disuse atrophy" protocol. Specifically, this will involve a repeating cycle of 5 second stimulation with 12 seconds recovery for a total of 20 minutes. Although you will be able to control the intensity of the stimulation based on tolerance, you are not to exceed 75% intensity on any training day. We will provide a recommendation based on how your muscles respond to the stimulation on the initial visit. Following the completion of this initial exercise protocol, the sticky electrodes will be removed and placed over the hamstring muscle group (back of the thigh on each limb as demonstrated in the initial meeting. A similar exercise protocol will then be conducted for the hamstring muscle group. This exercise session will take place with an investigator observing and audio and video recording via Microsoft Teams software through your phone or computer to provide instruction/support and to assess the quality of the exercise. Throughout the day reminders for the questionnaires will be sent through the PowerDot application.

4 weeks of exercise- Following that initial exercise day, you will be asked to continue to perform the exercise for 4-weeks 5 days per week at your home. Each exercise session will be identical to the single exercise session described above with the exception that the duration of the protocol may increase from 20 to 30 minutes depending on how you progress throughout the 4 weeks. Throughout this 4-week intervention, you will complete 1 questionnaire each day you exercise (this will take less than 1 minute). You will also complete the other 4 questionnaires on the 10th and last day of exercise (this will take 15-20 minutes). All questionnaires throughout this investigation will be administered through a web based software called Qualtrics. This will simply require you to click on a link on your computer, tablet or phone and answer the questions. Again, you will be reminded of their exercise and questionnaires through notifications in the PowerDot smartphone application. As previously mentioned, the initial exercise sessions will be observed by the investigator via Microsoft Teams to provide support/instruction. Remaining exercise sessions can also be observed by the investigator if you are still not comfortable operating the system on your own. Exercise session 10 and 20 will be observed and audio and video recorded by the investigator via Microsoft teams to assess quality of exercise session. The investigators will contact you if you fail to complete documents at required time or you are not completing the exercise sessions.

Benefits

Home based electrical stimulation

KENT STATE UNIVERSITY

By participating in this investigation, you will receive free home-based exercise for 4 weeks. Furthermore, your participation in this study will allow for a greater understanding of how electrically stimulated exercise can impact mood, emotion, and quality of life in individuals with SCI. The information garnered form this study can help to further our knowledge on how to best prescribe and deliver exercise to individuals with spinal cord injury to promote a healthy and meaningful lifestyle. If you complete the 4 weeks of exercise and you feel like you will use the PowerDot system in the future it is yours to keep.

Risks and Discomforts

All risks associated with this study are considered to be minimal. Furthermore, all available precautions will be taken to minimize these risks and discomforts.

Exclusion from the study: During the initial orientation meeting we may learn that your muscles do not respond to the stimulus. If this occurs, you will not be able to participate in the study. Individuals with injuries below T12 or who do not have muscles spasms are more likely to be non-responders and may want to consider this prior to scheduling the orientation meeting.

Surface Electrode Skin Irritation: When surface electrodes are used, it is possible that you will experience a temporary redness/irritation on your skin from the adhesive used to secure them. This redness should go away shortly after the electrodes are removed. If the redness/irritation continues to get worse from day to day, you may be removed from the study.

Skin burn: With electrical stimulation it is possible to receive a skin burn. This protocol has minimized this risk through the following: limiting stimulation intensity on the powerdot app to no more than 50%, discarding pads after 15 uses and encouraging proper storage and use of pads with informational sheet that will be provided to you. If you experience a burn please contact study staff immediately.

Uncomfortable Sensation: The PowerDot system will be delivering electrical pulses to the muscles in your lower limbs. In individuals without SCI electrical stimulation of a muscle may be perceived as a twitching sensation and if the stimulus intensity is too high it would be painful. However, the sensation you will receive will be dependent on the level and extent of your injury. During the initial meeting we will determine what stimulation intensity is best for you based on how your muscles respond and your tolerance to the stimulation. During the exercise sessions, you will have complete control of the level of intensity and you will be able to turn it down or off if it becomes uncomfortable.

Autonomic Dysreflexia: There is minor risk for subjects to develop autonomic dysreflexia during the exercise. AD is a reflexive increase in blood pressure caused by a noxious stimulus below the level of the injury in those with SCI. The risks are minimal because the stimulation is not constant, rather it is on for 5 seconds and off for 12. We will not be monitoring blood pressure as you will be performing this exercise at home, however other signs of AD that you should be aware of include: sweating, goosebumps and blotchy skin above the level of injury, headache and nasal congestion. If you do develop signs of AD you should simply turn off the stimulator and the AD will go away. Please contact the research staff if you develop any of these signs/symptoms during exercise. The subsequent exercise session will occur in the presence of a research staff via Microsoft Teams. You will be removed from the investigation if these

signs/symptoms develop during exercise a second time. If you have a history of developing AD, we will exclude you from this investigation.

Feeling of depression or anxiety: Several of the questionnaires will focus on depression, anxiety and mood states. Thus, these questionnaires may trigger uncomfortable and potentially harmful feelings. If you need help with depression or have thoughts of self-harm please contact the following helpline. This contact information will also be provided to you following those questionnaires.
National Alliance on Mental Illness: www.namigreatercleveland.org Please call 1-216-875-0266 for non-life threatening support. Call the suicide prevention lifeline at 1-800-273-8255 if you are having thoughts of harming yourself or others.

If at any time during the study you feel discomfort or that you do not want to continue, please inform the researcher. You may discontinue participation at any time. You should report any discomforts or adverse effects perceived to be a result of participation in this study immediately study personnel (contact information
below).

Privacy and Confidentiality

The results of this study will be published as a group as part of scientific publications. No individual results will be published or shared with any person or party preventing the release of your identity. You will select an ID code, and all data collected in relation to this study will linked with this ID code. The only piece of identifying data that will be collected will be your informed consent. Each of these forms will be kept separate from all other data and data will not be linked to you. The signed consent forms and medical history will be kept for 3 years after the research is complete per federal guidelines. All other research records will be stored securely for 3 years in another location, and only researchers and individuals responsible for research oversight will have access to the records. It is possible that the consent process and data collection will be observed by research oversight staff responsible for safeguarding the rights and wellbeing of people who participate in research. Finally, due to the nature of the internet and online activity there is a possibly that an unauthorized third party (i.e. a hacker) may view information that can identify you without authorization. Audio and video recording will take place on days 1, 10 and 20 to assess the quality of the exercise. We only need to capture your legs in the video and your face can be omitted. These files recordings will be deleted after analysis has been performed.

Voluntary Participation

Taking part in this research study is entirely up to you. You may choose not to participate, or you may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled. You will be informed of any new, relevant information that may affect your health, welfare, or willingness to continue your study participation.

Retainment of Contact Information for Future Studies

In the future we may have additional studies that might interest you. Can we keep you name and contact information (phone number and email address) available so we can contact you regarding these opportunities.

_____ YES _____ NO _____ INITIALS

Contact Information

If you have any questions or concerns about this research, you may contact:

John McDaniel, PhD
Kent State University
Phone: 801-598-7252; Email: jmcdani5@kent.edu

Cody Dulaney, ABD
Kent State University
Email: cdulane1@kent.edu

Consent Statement and Signature

I have read this consent form and have had the opportunity to have my questions answered to my satisfaction. I voluntarily agree to participate in this study. I understand that a copy of this consent will be provided to me for future reference.

_____ _____

Participant Signature **Date**

APPENDIX B.

HEALTH HISTORY QUESTIONNAIRE

Health History Questionnaire Subject code:_____

What was the date of your injury? _____

What is the level of your injury? _____

Prior to your injury, would you have considered your self a physically active individual? Explain

_____

_____

Were you involved in an exercise program prior to COVID19?

_____ 0 days per week _____ less than 15 minutes per session

_____1-2 days per week _____15-30 minutes per session

_____3-4 days per week _____30-45 minutes per session

_____ 5-7 days per week _____ greater than 45 minutes per session

What did this involve _____

_____

_____

Are you currently involved in an exercise program? If so explain?

_____ 0 days per week _____ less than 15 minutes per session

_____1-2 days per week _____15-30 minutes per session

_____3-4 days per week _____30-45 minutes per session

_____5-7 days per week _____ greater than 45 minutes per session

What does this involve? _____

_____

_____

Have you used muscle stimulation in the past? If so explain.

_____

_____

_____

Do you have spasticity in your lower limbs? _____yes ____ No If so how often, and does it hinder your activities of daily living? _____

_____

Do you have an internal cardiac pacemaker, defibrillator or any other internal electrical device? _____

_____

Do you have a history of developing autonomic dysreflexia? If so please explain.

_____

_____

_____

Do you have any existing pressure sores? _____

Do you typically have skin sensitivity to band-aids or adhesives? _____

Do you have any current lower limb musculoskeletal injuries? Explain. _____

_____

_____

APPENDIX C.

INSTITUTIONAL REVIEW BOARD APPLICATION

KENT STATE UNIVERSITY

IRB LOG NUMBER: 20-430

Use of Human Subjects in Research Application

(LEVEL II or LEVEL III projects)

THIS SECTION FOR USE BY IRB	*Date received by ORC*	Revised 11/16/20
Name of discipline -specific reviewer: A. Ridgel		

Level of review (please choose either Expedited or Full board)

☒ ***Level II – Expedited Review***

Please specify one or more category:

- ☐ - #1 - Clinical Studies
- ☐ - #2 - Collection of Blood Samples
- ☐ - #3 - Pros collection of Bio Specimens
- ☒ - #4 - Data through non-invasive procedures.
- ☐ - #5 - Materials (Data, documents, records or specimens collected for non-research purposes)
- ☐ - #6 - Data from voice, video, digital or image recordings
- ☐ - #7 - Individual or group characteristics

☐ **Level III – Full Board Review**

Continuing Review:

☒ **Three-year check-in: 11/16/20-11/15/23**

☐ **Annually:**

☐ **Other:**

Notes:

External Funding: ☒ No ☐ Yes

Stamped Consent: ☐ No ☒ Yes: **11/16/20-11/15/23 (1)**

Agenda Date: 1/13/20

CR Reminder Sent: ☐ No ☐ Yes

INSTRUCTIONS FOR INVESTIGATORS:

1. Submit this completed document with any needed attachments via email attachment to an IRB discipline specific reviewer.

   This form must be submitted from the Principal Investigator's @kent.edu email account.

   Submission of incomplete forms or failure to include all of the needed attachments will likely result in delays for IRB review/approval. Handwritten forms are not accepted.

   Single left-click to complete text fields.

   To check a box, double left-click on the box, then click "checked". Click OK.

2. Do NOT begin data collection prior to receiving notification from the KSU IRB that the study has received final approval.

Section 1 – TITLE & PRINCIPAL INVESTIGATOR (PI) INFORMATION

1a. Title of Study: *The effect of home-based electrical stimulation exercise on depression, anxiety and quality of life in those with SCI.*

1b. Estimated begin and end dates for the project	Oct 2020 to Oct 2021
1c. Name: John McDaniel, PhD	Status: ☒ Faculty ☐ Staff
1d. Phone: (330) - 672 -0802 or extension	Department: EXSC
1e. Purpose of Research: ☐ Faculty Research ☒ Student Thesis/Dissertation → Complete Appendix A ☐ Other: Specify:	PI Email: Jmcdani5 @kent.edu

Only faculty members and professional staff who are full-time university employees are eligible for PI status. Please review IRB policy for PI eligibility and responsibilities.

1g. Email address(es) for others that should be notified regarding the status of this application (i.e., student(s) conducting research, program administrators, etc.):	Cdulane1 @kent.edu @kent.edu

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