CARDIORESPIRATORY FITNESS, PHYSICAL ACTIVITY, AND PSYCHOLOGICAL EFFECTS OF AN ACUTE BOUT OF CYCLING EXERCISE IN PEOPLE WITH EPILEPSY

by

KRISTEN E. JOHNSON

(Under the Direction of Patrick J. O'Connor)

ABSTRACT

The primary purpose of this study was to test if an acute bout of cycling exercise in a sample of adults with epilepsy would improve feelings of energy and enhance executive functioning. Secondary aims included evaluating cardiorespiratory fitness and physical activity levels. A within-participants crossover design was used to compare seated rest to 20 minutes of moderate-intensity cycling. Ten people diagnosed with epilepsy completed the Profile of Mood States (POMS) and the Wisconsin Card Sorting Task (WCST) before and twice after the treatments. Within-participants repeated measures ANCOVAs, controlling for initial values, showed a significant interaction for POMS vigor, $F(2,32)=4.21$, $p=.024$, $\eta^2=.208$; immediately after exercise, vigor scores were higher than seated rest. WCST performance was not influenced by acute exercise. Acute exercise results in transient increases in feelings of energy without altering executive functioning.

INDEX WORDS: epilepsy, exercise, physical activity, cardiorespiratory fitness, executive function, cognitive function, mood,

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DEDICATION

To my village: every positive vibe sent, every word of encouragement uttered, and every ounce of faith placed in me when I had little faith in myself, has sustained me and given me strength. Thank you.

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CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

Epilepsy is defined as the predisposition to generate seizures resulting either from excessive neuronal excitation or from inadequate neuronal inhibition caused by structural and/or metabolic brain abnormalities [1].

Epilepsy is among the most common neurological conditions, affecting nearly 65 million people worldwide [2] and 2.3 million people in the United States [3]. In addition to seizures, most people with epilepsy also report at least one comorbid condition such as anxiety, asthma, depression, and chronic pain, with nearly 40% reporting more than four comorbid conditions [4]. Comorbid conditions with epilepsy contribute to the disease burden, increase health-care costs, impact clinical outcomes, negatively influence quality of life, and contribute to premature mortality [4].

The brain abnormalities that cause epilepsy, along with anti-seizure drug side effects, may also contribute to the increased risk for psychiatric comorbidity in people with epilepsy, as epilepsy is consistently associated with an increased prevalence of mood disorders, anxiety disorders, and cognitive deficits [5]. The exact pattern of cognitive impairment depends on the individual's epilepsy diagnosis. For example, an individual with focal, frontal-lobe epilepsy will likely experience impairment in cognitive functions associated with the frontal lobe [6]. Impairment in people with generalized epilepsies may experience sub-clinical but significant impairment in a variety of cognitive functions including general intelligence, crystallized and fluid intelligence, long and short term memory, cognitive processing speed, and executive function [7].

Seven cross sectional studies based in the United States and Canada have explored the relationship between epilepsy and self-reported physical activity in adults [8-14]. Five of the seven studies found that people with epilepsy are significantly less active compared to the general population [8, 10-12, 14]. One nationally representative study exploring health habits of 27,139 people in the United States found that people with a history of epilepsy were less likely to meet physical activity guidelines than people with no history of epilepsy (39.1% vs. 46.3%. respectively) [11].

It is unfortunate that people with epilepsy appear to be less active than the general population. Though the evidence that regular exercise improves seizure control in people with epilepsy is currently limited, there is abundant evidence suggesting that physical activity may be of most benefit in improving the quality of life in people with epilepsy, in part by alleviating comorbid disorders and anti-epileptic drug side effects. Growing evidence in samples of people without epilepsy demonstrates that physical activity is effective in attenuating several epilepsy comorbidities including, hypertension [18], diabetes [19], back pain [20], depression [21], and anxiety [22]. People with epilepsy may experience similar benefits from participating in physical activity.

A single bout of exercise may also be beneficial for people with epilepsy. Significant reductions in the number of epileptic discharges during or immediately following exercise have been observed in people with temporal lobe epilepsy [23], and juvenile myoclonic epilepsy [24]. As with chronic exercise, acute bouts of aerobic exercise are effective in relieving some signs and symptoms of comorbidities in people without epilepsy including blood pressure reduction in hypertensive patients [25], increased insulin sensitivity in people with type 2 diabetes [26], reduced depression symptoms [27], and fewer anxiety symptoms among people with elevated symptoms [28]. In people without epilepsy, an acute bout of exercise has its most consistent and largest effect on the mood state of vigor. Acute exercise often has little effect on the mood states of confusion and anger. Acute exercise often reduces state anxiety, but state anxiety is also reduced in passive control conditions such as seated quiet rest [28]. Whether these responses occur after acute exercise or seated rest for people with epilepsy is unknown.

People without epilepsy benefit psychologically from even a single bout of exercise, but the extent to which those benefits extend to people with epilepsy remains unexplored. The present investigation seeks to gather science-based information from people with epilepsy about: the psychological consequences of a single bout of exercise. Existing evidence suggests that people with epilepsy will experience improved feelings of energy and improved cognitive function following an acute bout of exercise compared to seated rest.

Chapter 2 of this thesis provides background information on epilepsy, and reviews the evidence related to physical activity and exercise in people with epilepsy.

Chapter 3 of this thesis describes an experiment conducted to compare the mood and cognitive effects of an acute bout of moderate-intensity exercise to seated rest in young adults with epilepsy.

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CHAPTER 2

LITERATURE REVIEW

2.1 EPILEPSY DEFINED

Epilepsy is the predisposition to generate seizures resulting from either enhanced neuronal excitation or a failure of adequate neuronal inhibition [1]. To be diagnosed with epilepsy, one must have had two or more unprovoked seizures occurring at least 24 hours apart, which are independent of other illnesses. A distinction is often made between active and inactive epilepsy. A person with active epilepsy is one who is currently being treated for epilepsy or who has had at least one seizure within the past five years. People with inactive epilepsy have been diagnosed with epilepsy in their lifetime, but have not had any seizures within the last five years and are not currently being treated for the disorder. A solitary epileptic seizure, febrile seizures, neonatal seizures, and seizures resulting from systemic insults (e.g., alcohol abuse) are typically not considered to be epilepsy [2].

2.2 PREVALENCE OF EPILEPSY

Epilepsy is a common neurological disorder affecting more than 65 million people worldwide [3] and approximately 2.3 million people in the United States [4]. U.S. prevalence estimates range from 1.3% to 2.1% among adults [5-12]. The prevalence of epilepsy is generally higher in developing countries and among poorer groups in developed countries, possibly due to greater population exposure to epilepsy risk factors such as infections and inadequate neonatal and perinatal care [13]. Epilepsy is most prevalent in children younger than one year old and in adults older than 65. There is no difference in epilepsy prevalence between men and women [14].

2.3 IMPACT OF EPILEPSY

2.3.1 Mortality

People with epilepsy have a risk of premature death that is roughly 3 times greater than in the general population [15, 16]. Risk of premature death is elevated in individuals with poor seizure control and higher seizure frequency. Premature death in epilepsy may be a direct result of seizure-related complications such as sudden unexpected death in epilepsy, which accounts for almost 2% of deaths among those with epilepsy [15]. Premature death may also be attributable to elevated risk for comorbid diseases [16]. Even when in remission, people with a history of epilepsy are twice as likely to die early [17].

2.3.2 Cost

Epilepsy can be a costly neurological disorder. While healthcare costs associated with epilepsy vary by epilepsy sub-population (epilepsy etiology, severity, and type), estimates of direct, epilepsy-specific costs have a wide range, from $1,022 to $19,749 per person each year in the United States, accounting for $2.4 billion to $45.4 billion in total healthcare costs annually [18]. Cost of anti-epileptic drugs are the largest component of the direct cost of epilepsy, accounting for between 11% and 71% of total cost [18]. Costs tend to be higher in patients with uncontrolled epilepsy, and in patients with poor treatment adherence [18].

2.4 CAUSES OF EPILEPSY

The International League Against Epilepsy classifies the causes of epilepsy into the following categories: genetic, structural/metabolic, and unknown [19]. Epilepsy's genetic component has been well established, with monozygotic twins demonstrating greater concordance for the disorder than dizygotic twins. Additionally, individuals with a close relative with the disorder have 5 times elevated risk of developing epilepsy compared to those without a close relative with epilepsy [20]. While specific genes and combinations of genes have been identified as being possible causes for the development of epilepsy, these represent only a small portion of epilepsy cases [1]. In most cases, a specific genetic cause remains unidentified.

Structural and metabolic abnormalities may also enhance one's risk of developing epilepsy. These characteristics may be of genetic origin such as those resulting from cortical malformation during development, or may be brought about by an acquired condition such as tumors, traumatic brain injury, infectious disease, autoimmune disease, or stroke [20].The cause of epilepsy is unknown is roughly 60% of all cases [21].

2.5 EPILEPSY COMORBIDITIES

Comorbid conditions in epilepsy contribute greatly to the disease burden, increase health-care costs, and negatively impact clinical outcomes, mortality risk, and quality of life [22]. This poses a significant problem, as more than 60% of adults with epilepsy report at least one comorbid condition, and more than 40% of people with epilepsy report more than four [23].

Most somatic disorders comorbid with epilepsy are either caused by epilepsy or are a result of seizures or anti-epileptic drug use, or can contribute to epilepsy. For example, heart disease, high blood pressure, and type 2 diabetes are more commonly found in people with epilepsy than in people with no history of epilepsy [24], and all are risk factors for stroke, which is one possible cause of epilepsy [25]. Similarly, a history of stroke and cancer are more commonly found in people with epilepsy, as they are both possible causes for epilepsy [25].Other disorders more commonly found in people with epilepsy than in people without epilepsy include asthma and arthritis, but their causal relationship with epilepsy remains unknown [25].

The structural and metabolic brain abnormalities that cause epilepsy may also contribute to an increased risk for neurobehavioral comorbidities. Epilepsy is consistently associated with an increased prevalence of mood disorders, anxiety disorders, and cognitive deficits [26]. The patterns of cognitive impairment can depend on the individual's epilepsy diagnosis. For example, individuals presenting with focal, frontal-lobe epilepsy will often experience impairment in cognition that corresponds with the location of their epilepsy (e.g., executive function) [27]. A meta-analysis evaluating cognitive impairment in idiopathic generalized epilepsies described cognitive impairment as being sub-clinical but still significant, with impairments in multiple domains of cognition including general intelligence, both crystallized and fluid intelligence, long term and short term memory, cognitive processing speed, and executive function [28].

While many comorbidities of epilepsy may be managed pharmacologically, regular physical activity should also be considered as a possible treatment or adjunct. Growing evidence demonstrates that physical activity is effective in attenuating several epilepsy comorbidities including cardiovascular disease risk factors, depression and anxiety disorders, and cognitive deficits [29-32].

2.6 EPILEPSY TREATMENT

The primary goal of epilepsy treatment is to control seizures while minimizing adverse effects. Though surgery may ultimately be required, this is most commonly accomplished through the use of anti-epileptic drugs, which primarily function either by increasing neuronal inhibition through enhancement of the gamma-aminobutyric acid neurotransmitter system or by decreasing neuronal excitation through the blocking of sodium channels. However, anti-epileptic drugs are only effective in 60-70% of epilepsy patients, leaving more than 30% of patients with uncontrolled seizures. Even patients who experience successful seizure control through pharmacological intervention may suffer from harmful side effects of anti-epileptic drugs including low bone density [33], weight gain [34], depression, and anxiety [35]. Side effects most commonly associated with a wide range of anti-epileptic drugs include drowsiness, dizziness, nausea, low bone mineral density, and increased risk of bone fracture [36].

2.7 PHYSICAL ACTIVITY IN PEOPLE WITH EPILEPSY

At least 7 epidemiological studies, based primarily in Canada and the United States, support that people with epilepsy are less physically active than the general population [37]. However, all of these studies used self-reported physical activity which may over-estimate vigorous physical activity and under-estimate sedentary time compared to objective measures such as accelerometry [38]. Physical inactivity can contribute to low cardiorespiratory fitness, and low cardiorespiratory fitness at age 18 increases the risk for epilepsy later in life [39]. However, there appears to be no prior research quantifying cardiorespiratory fitness levels among people with epilepsy

2.8 EFFECT OF EXERCISE IN PEOPLE WITH EPILEPSY

2.8.1 Chronic Exercise

Regular exercise may prove to be an effective complementary treatment for epilepsy; however, evidence that exercise training improves seizure control in people with epilepsy is currently weak. There are only three studies evaluating the effect of adopting a regular exercise program on seizure frequency, and the results are mixed. Of the two uncontrolled studies, one reported reduced seizure frequency during a 15-week exercise intervention [40], and the other reported no change in seizure frequency [41]. One small randomized controlled experiment explored the effects of physical activity on seizure control, and it found that people with epilepsy who adopted a physical exercise program for 12 weeks showed no change in seizure frequency [42].

Physical activity may be of most benefit in improving the quality of life in people with epilepsy, in part by alleviating comorbid disorders and anti-epileptic drug side effects. Growing evidence in samples of people without epilepsy demonstrates that physical activity is effective in attenuating several epilepsy comorbidities including, hypertension [43], diabetes [44], back pain [45], depression [30], and anxiety [31]. Whether regular physical activity is associated with, or causally improves, these common comorbid conditions in people with epilepsy is unknown.

2.8.2 Acute Exercise

A single bout of exercise may also be beneficial for people with epilepsy. Significant reductions in the number of epileptic discharges during or immediately following exercise have been observed in people with temporal lobe epilepsy [46] and juvenile myoclonic epilepsy [47]. As with chronic exercise, acute bouts of aerobic exercise are effective in relieving some signs and symptoms of comorbidities in people without epilepsy including blood pressure reduction in hypertensive patients [48], increased insulin sensitivity in people with type 2 diabetes [49], reduced depression symptoms [50], and fewer anxiety symptoms among people with elevated symptoms [51].

In people without epilepsy, an acute bout of exercise transiently improves psychological well-being and cognitive function. The most consistent of these psychological effects appear to be improvement in executive function [52-55] and increases in feelings of energy [56]. Acute exercise can also reduce state anxiety, and the effect is largest for those with elevated anxiety symptoms [50].Whether these psychological benefits occur, are augmented, or are attenuated after acute exercise among people with epilepsy is unknown, in part because people with epilepsy have historically been excluded from participating in exercise studies.

2.9 SUMMARY

Epilepsy is one of the most common neurological disorders in the world with extensive negative effects on health and quality of life. Epilepsy comorbid disorders and side effects related to anti-epileptic drug use significantly contribute to the disease burden. The evidence that regular physical activity may improve seizure control in people with epilepsy is weak, but it may be more effective in alleviating comorbid disorders, thereby enhancing quality of life in people with epilepsy. Epileptiform activity monitored by electroencephalography is significantly reduced both during and after acute bouts of physical activity which supports the safety of acute and chronic exercise among people with epilepsy. People without epilepsy benefit psychologically from even a single bout of exercise, but the extent to which those benefits extend to people with epilepsy remains unexplored. There is a need for science-based information from people with epilepsy about: 1) the psychological consequence of a single bout of exercise, 2) objectively measured physical activity, and 3) cardiorespiratory fitness levels.

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CHAPTER 3

CARDIORESPIRATORY FITNESS, PHYSICAL ACTIVITY, AND PSYCHOLOGICAL EFFECTS OF AN ACUTE BOUT OF CYCLING EXERCISE IN PEOPLE WITH EPILEPSY[1]

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3.1 ABSTRACT

Purpose: The primary purpose of this study was to test if an acute bout of cycling exercise in a sample of young adults with epilepsy would improve feelings of energy and enhance cognitive (executive) function. Secondary aims included evaluating cardiorespiratory fitness and physical activity level. **Methods:** A within-participants crossover design was used to compare seated rest to 20 minutes of moderate-intensity cycling. Ten people diagnosed with epilepsy completed the Profile of Mood States (POMS) and the Wisconsin Card Sorting Task (WCST) before and twice after the treatments. Cardiorespiratory fitness was assessed with a standardized, graded maximal cycling exercise test. Physical activity level was assessed with a hip-worn accelerometer (ActiGraph GT3X+) and a self-reported past-year physical activity questionnaire (CARDIA Physical Activity History). **Results:** Within-participants repeated measures ANCOVAs, controlling for initial values and order of treatments, showed a significant interaction for POMS vigor, $F(2,32)=4.21$, $p=.024$, $\eta^2=.208$; immediately after exercise, vigor scores were higher than seated rest. WCST performance was not influenced by acute exercise. Independent t-tests revealed that this sample of people with epilepsy was similarly fit and similarly physically active compared to reference groups of young adults without epilepsy. **Conclusion:** Acute exercise results in transient increases in feelings of energy without altering executive functioning.

3.2 INTRODUCTION

Epilepsy is a common neurological condition, affecting nearly 65 million people worldwide [1] and 2.3 million people in the United States [2]. People with epilepsy have a predisposition to generate seizures resulting either from excessive neuronal excitation, or from inadequate neuronal inhibition, caused by structural and/or metabolic brain abnormalities [3].

The brain abnormalities that cause epilepsy, along with anti-seizure drug side effects, are associated with increased risk for chronic health problems (e.g., asthma, heart disease) [4], including psychological comorbidities. Epilepsy is associated with an increased prevalence of mood disorders, anxiety disorders, and cognitive impairments such as language problems and deficits in attention and executive function [5]. Physical inactivity is a possible contributing factor to these chronic health problems in people with epilepsy [6].

The health consequences of physical inactivity among people with epilepsy are poorly understood. Self-reported physical activity levels appear to be low in people with epilepsy. At least seven cross sectional studies based in the United States and Canada have explored the relationship between epilepsy and self-reported physical activity in adults [7-14]. Five of the seven studies found that people with epilepsy are significantly less active compared to the general population [7, 9-11, 13]. One nationally representative study exploring the health habits of 27,139 people in the United States found that people with a history of epilepsy were less likely to meet physical activity guidelines than people with no history of epilepsy (39.1% vs. 46.3%. respectively) [10]. However, there appear to be no studies in which objective indicators, such as accelerometry or cardiorespiratory fitness, were used to assess the physical activity levels of people with epilepsy with less bias than self-reported measures [15].

Compared to the general population, people with epilepsy have additional barriers to participating in physical activity. These barriers include concerns about the safety of physical activity expressed by family or health care providers [16], a personal fear of an exercise-induced seizure [17], and feelings of low energy [18]. Despite these perceptions, the evidence shows that the number of epileptic discharges measured with electroencephalography during or immediately following exercise are reduced in people with temporal lobe epilepsy [19] and juvenile myoclonic epilepsy [20]. Experts have concluded that the risk of a seizure is decreased during exercise [21]. A single bout of exercise also consistently increases feelings of energy in people without epilepsy, especially in those with low energy [22]. Moreover, after people without epilepsy complete a single bout of exercise, they often report reduced symptoms of anxiety [23] and depression [24], and show improvements in cognitive function, especially executive function [25-27].

Whether people with epilepsy benefit psychologically in response to a single bout of exercise, or whether the usual mood (e.g., increased feelings of energy) and cognitive (e.g., improved executive function) benefits are prevented either because of their neurological condition or the medications they are taking [28], is unknown. The primary aim of this investigation was to test the hypothesis that, compared to a non-exercise rest condition, feelings of energy and executive function performance would improve after 20 minutes of moderate-intensity exercise in people with epilepsy. The secondary aim was to obtain objective measures of physical activity and cardiorespiratory fitness and make comparisons to the best available reference groups of people without epilepsy of the same age.

3.3 METHODS

3.3.1 Sample

Participants were recruited for a research study of physical activity, cardiorespiratory fitness, and the acute effects of exercise on selected psychological outcomes in people with epilepsy via list-servs, in-class presentations, flyers, advertisements, and word of mouth. Participants were included if they: (i) were 18-29 years old, (ii) were diagnosed with epilepsy by a doctor, (iii) had at least one seizure within the past 10 years, (iv) had stable seizure medication, if used, for six or more months, and (v) provided a physician's consent to participate because they had a seizure during the past year. Potential participants were excluded from the study if they had any contraindications to maximal exercise. The epilepsy-related inclusion and exclusion criteria were based on task force recommendations of leading epilepsy researchers and clinicians, which are based on epidemiological, experimental, and clinical evidence available from January 1950 through March 2015[21]. Participants received $40 compensation for their completion of laboratory testing.

3.3.2 Procedure

Baseline – Day One

Timing of study procedures is presented in Table 3.1. On day one, participants reported to the laboratory and were read the informed consent document which explained the purpose of the study, experimental procedures, risks and benefits of participating, and confidentiality of the data obtained. Participants were asked if they had any questions or concerns regarding the study, and signed the informed consent. Next, an online questionnaire to assess the participants' physical activity history was completed. Participants also completed an online version of the SF-36 Health Questionnaire. Then, participants performed a practice trial of the cognitive task. Performance on the cognitive task was checked to ensure that participants understood the instructions. No participants scored more than two standard deviations below norms, and therefore were not asked to complete additional practice trials. After completing the online questionnaires and cognitive task, participants completed a graded maximal leg cycling exercise test to assess cardiorespiratory fitness. After recovery from the exercise test, participants were issued one accelerometer with instructions to wear it on the dominant hip during waking hours for one week. The next visit was scheduled, and participants were asked to return with the accelerometer at their scheduled date and time prepared to complete 20 minutes of submaximal exercise.

Experimental Days – Days Two and Three

At least one week after completing baseline assessments, participants reported to the laboratory for Day Two. Participants returned the accelerometer and then completed the first mood questionnaire and cognitive task online. After completing the initial assessment, participants were randomly allocated to one of two conditions: 20 minutes of moderate intensity exercise or seated rest. Immediately post-condition, participants completed the online mood questionnaire and cognitive task a second time. Following a five minute break, participants completed the mood questionnaire and cognitive task a final time. Day Three was completed at least 48 hours following Day Two. All Day Three procedures were identical to Day Two except for the condition allocation.

3.3.3 Screening Questionnaires

Participants were screened for eligibility using two questionnaires presented online. The Physical Activity Readiness Questionnaire (PAR-Q) is an eight-item questionnaire used to determine if an individual has contraindications to exercise [29] (Appendix A). If a potential participant answered “yes” to any PAR-Q items, he/she was excluded from study participation.

A questionnaire was developed and used to gather demographic and epilepsy history information (Appendix B).

3.3.4 Physical Activity Measures

Accelerometer

The ActiGraph GT3X+ accelerometer was used to objectively measure free-living physical activity in each participant. The dimensions and the weight of the accelerometer are 4.6 cm X 3.3 cm X 1.5 cm and 19 grams, respectively. Participant data were recorded in one-minute epochs. A sampling rate of 100Hz was used. The accelerometer was worn on the anterior of the dominant hip during waking hours with the request to wear it for at least one week during all waking hours. The times of day the participants put the monitor on and took the monitor off were recorded in a log. Four days with at least 10 hours of wear time, including at least one weekend day, was required for an individual’s data to be included in the analyses. Average weekly time spent in light, moderate, vigorous, and combined moderate-to-vigorous physical activity for both weekdays and weekends was calculated for each participant [30]. Average daily time spent in light, moderate, vigorous, and combined moderate-to-vigorous physical activity across all valid days was calculated using a previously described method [31].

CARDIA

The CARDIA Physical Activity History Questionnaire assesses self-reported recalled physical activity during the past 12 months and takes 5-10 minutes to administer [32] (Appendix C). Frequency and intensity information yielded exercise units which are reported here for moderate, vigorous, and total physical activity. Three hundred total exercise units approximates an energy expenditure of 1,500 kcal/week [33]. Physical activity estimated from the CARDIA has shown moderate positive correlations with cardiorespiratory fitness and moderate negative correlations with body fat percentage [32].

3.3.5 Cardiorespiratory Fitness

Procedure

Participants were fitted with a Polar heart rate monitor and a face mask to measure expired gases and volumes. Using open circuit spirometry, expired air was collected and analyzed by a Parvo Medics TrueOne 2400 Metabolic Measurement System (Parvo Medics, Inc., Sandy, UT) to determine rates of oxygen uptake and associated cardiorespiratory and metabolic variables. Standard gases of known composition were used to calibrate the oxygen and carbon dioxide analyzers, and a 3-L syringe was used to calibrate the pneumotachometer prior to each testing session. Participants were given a 5 minute warm up period starting at 50 watts and asked to maintain a cadence of 60-80 revolutions per minute. After the warm up, the resistance was increased by 25 watts every 2 minutes until the participant was no longer able to continue at the prescribed resistance (RPM < 50 for > 10 sec). A 5-minute cool down with 25 watts resistance began immediately following the conclusion of the test. At the end of each exercise stage, overall ratings of perceived exertion and leg muscle pain intensity ratings were obtained and 60-second heart rate was recorded.

Heart Rate

A Polar heart rate monitor (Model T31) was used to assess the participants' heart rate during the graded maximal exercise test. Heart rate was assessed during each exercise stage and averaged across the final minute of each stage.

Perceptual Ratings

Ratings of perceived exertion were obtained using Borg's 6-20 scale. The responses range from 6 (no exertion) to 20 (maximal exertion). Participants were provided with standardized instructions for providing ratings of perceived exertion [34]. Overall ratings of perceived exertion were assessed during the last 10 seconds of each exercise stage. Ratings of perceived leg muscle pain intensity were also obtained immediately after each rating of perceived exertion using standardized instructions and a scale ranging from 0 (no pain at all) to 10 (extremely intense pain) [34].

3.3.6 Seated Rest

On their rest condition day, participants were asked to sit in a chair in a quiet room with the door closed for twenty minutes. Participants were instructed not to read, use any mobile device, or use the computer for the duration of their rest period. The rest period was timed with a stopwatch.

3.3.7 Submaximal Exercise

On their exercise day, participants walked across the hall (~13 feet) from the room where the mood and cognitive tasks were performed and into the room with the cycle ergometer. The bicycle seat was adjusted to the appropriate height for the participant, and s/he began cycling at a resistance estimated to produce 65% of their peak oxygen uptake while cycling at a cadence of 60-80 rpm [35]. The twenty minute exercise duration was timed with a stopwatch [35].

3.3.8 Executive Function - Wisconsin Card Sorting Task

The Wisconsin Card Sorting Task was used to assess executive function, especially the ability to adapt to changes (i.e., attentional set shifting) [36]. This task was chosen because people with epilepsy show reduced performance on executive function tasks and acute exercise improves executive function [25-27]. The objective of the task is to accurately sort a series of cards using a rule based on one of three characteristics of the cards: color, shape, or number. The sorting rule changed every 10 cards. The task required the participants to correctly identify the sorting rule, maintain accurate performance using the rule, inhibit the use of the previous rule once it no longer applied, and shift to the new rule once it applied. All participants in both conditions and for all measurement trials sat at a desk 24 inches from the same desktop computer running Microsoft Windows 7, version 6.1 and a 30.5cm x 38 cm monitor in a quiet room with the door closed. The computer accessed the psytoolkit.org website [37]. The following instructions preceded each test: *"In this task, your goal is to match the card presented at the bottom of the screen to one of four cards presented at the top of the screen. You will be given feedback after each card. Cards may be matched according to any of three rules: color, shape, or number... You will need to determine which sorting rule is being used, but be aware that the sorting rule will change periodically. You will need to carefully monitor your feedback in order to select the correct sorting rule. This task contains 60 trials."*

A screen-shot of the task is depicted in Figure 3.1. In the center of the computer screen and against a black background, four cards (1" x 1") were presented in a row. Each card had a grey background and depicted one of four shapes (circle, triangle, cross, or star), presented in one of four colors (red, yellow, blue, green). An additional card was presented at the bottom of the screen, and the participant guessed which rule was being used (shape, color, or number of objects) and indicated the guess by using a mouse to click on one of the cards in the row of four cards near the top of the screen. Correct responses resulted in the word "Good!" presented below the card. Incorrect responses result in the word "Wrong!" presented below the card. Each test consisted of a total of 60 trials, and the participant had 10 seconds to choose a decision rule for each card presented. Outcomes measured were the number of perseveration errors (errors caused by repeating a prior correct response after a new rule started), and average response time for the correct responses.

The Wisconsin Card Sorting Task – 64 card version most closely resembles the online version of the Wisconsin Card Sorting Task used in the present study. In order to make a better comparisons to published data, Wisconsin Card Sorting Task scores from this shorter (60 card) online version were converted to estimate scores for a version the length of the original test using the following formula: WCST Perseverative Errors = -.3915 + 1.8801 x WCST 64 Perseveration Errors [38].

The criterion measures were the raw number of perseveration errors, the estimated number of perseveration errors (using the formula described above), and the response time. Preliminary analyses examined the reliability (intraclass correlation) of response time data in the three correct trials before and after a rule change as well as for all correct trials. The reliability was above 0.70 for analyses that used a fewer number of trials but not as high as when all trials were used (ICC = .912). The ANCOVA results for response time were the same whether all trials were used or only the three correct trials after a rule change was used. All correct trials were used as the criterion measure in the response time analysis.

3.3.9 Mood – Profile of Mood States – Brief Form

The Profile of Mood States-Brief Form was used, and it is a 30 item questionnaire that assesses the intensity of six different moods: tension, depression, anger, confusion, vigor, and fatigue. Responses range from 0 (indicating not at all) to 4 (indicating extremely). Participants were instructed to report how they felt “right now, at this moment”.

3.3.10 Quality of Life

SF-36

Health related quality of life (a.k.a., perceived health status) was evaluated using the SF-36 Health Questionnaire [39]. The SF-36 consists of 36 questions, the answers to which are used to generate eight sub-scale scores. The sub-scales are: vitality, physical functioning, bodily pain, general health perception, physical role functioning, emotional role functioning, social role functioning, and mental health. Standardized scores range from 0 to 100 with the lower scores indicating more disability. Comorbid disorders were evaluated as an additional measure of quality of life. The self-administered comorbidity questionnaire evaluates the presence of 12 common medical conditions with the option of adding three additional conditions in an open-ended fashion. Number of comorbid conditions for each participant can range from 0 to 15. Severity of each condition is also evaluated on a scale of 1 to 3, and a comorbidity score is assigned with higher scores indicating more severity of present comorbid conditions. Total scores on this questionnaire range from 0 to 45 and have moderate associations with chart-review based comorbidity indexes [40].

3.3.11 Statistical Analyses

All collected data were entered into IBM SPSS (version 22.0.0). Condition (2: Exercise vs. Rest) x Time (3: Pre, Post 1, Post 2) repeated measures ANCOVAs tested the primary hypotheses (i.e., condition x time effects for vigor and Wisconsin Card Sorting Task performance). Treatment order and baseline scores were included as covariates. Bonferroni-adjusted dependent t-tests were used to understand significant interactions. The analysis used data on the full sample of women and men because of the low statistical power for detecting sex-related differences. Independent t-tests were used to compare cardiorespiratory fitness and physical activity levels of this sample to reference groups. The magnitude of effects was quantified using partial eta squared and Cohen's d [41]. Cohen suggested a d= 0.50 is a medium sized effect and others suggested that d values ≥ 0.5 indicate a clinically important effect [42].

3.4 RESULTS

3.4.1 Participants

Participant demographic and epilepsy history information is presented in Table 3.2. Ten participants (7 female) completed the study. Participants were young (20.50 ± 1.78, 19-24 years) and had a normal body mass index (20.81 ± 3.23). All participants had been diagnosed with epilepsy, though the cause of the seizures was unknown for most participants (*n*=8). Two participants indicated that their seizures were caused by an error in brain development. Almost all participants (*n*=9) were taking anti-seizure medication at the time of the study. Seven participants were taking one anti-seizure medication, one participant was taking two anti-seizure medications, and one participant was taking three anti-seizure medications. The most common anti-seizure medication in this sample was lamotrigin (*n*=4), followed by levetiracetam (*n*=2) and oxcarbazepine (*n*=2). The most commonly reported side effects from anti-seizure medication were dizziness (*n*=3) and drowsiness (*n*=2), and memory problems (*n*=2). Overall participants' seizures were well controlled with 7 participants reporting no seizures per usual month in response to the question: "How often do you have seizures?" (range = 0 to 3). Half of the sample reported a seizure within the last year, and the other half reported their last seizure from 3 to 8 years before participating in the study.

3.4.2 Quality of Life

Participants reported an average of 1 comorbid condition. The most common comorbid conditions present in this sample were depression (*n*=3) and back pain (*n*=2). The SF-36 data are presented in Table 3.3. In most SF-36 domains, this sample was similar to a group of 173 individuals, aged 18-24, whose data are provided in the SF-36 manual [39]. Compared to this normative group, the present sample scored insignificantly higher (better) on physical and social function, insignificantly lower (worse) on vitality, and significantly lower (worse) in the general health domain, $t(181) = 2.85$, $p=.005$.

3.4.3 Cardiorespiratory Fitness and Physical Activity

Fitness and physical activity data are reported in Table 3.4. Seven participants completed a valid graded maximal exercise test on a cycle ergometer. Maximal cycling exercise did not produce any obvious seizures. The group average (± SD) test duration was 496 ± 185 seconds. The group reported a peak perceived exertion of 16.14 ± 1.08 and a peak leg pain intensity of 6.00 ± 1.23. The group peak heart rate was 184.14 ± 6.74 beats·min^{-1}, peak respiratory exchange ratio was 1.21 ± .05, and peak oxygen uptake was 30.67 ± 6.98 ml•kg^{-1}•min^{-1}.

Peak exercise test results for the five women were 27.26 ± 3.52 ml•kg^{-1}•min^{-1}(95% CI: 24.16 – 28.87), 181.40 ± 5.55 bpm, with a respiratory exchange ratio of 1.20 ± 0.05 and perceived effort of 15.00 ± 2.45. Peak oxygen uptake for the females was moderately, but statistically insignificantly, lower than cardiorespiratory fitness in a reference group of 235 women aged 20-29 who completed a graded maximal exercise test on the cycle ergometer, $t(238)=0.84$, $p=.402$, $d=-0.50$ [43].

Peak exercise test results for the two men were 39.20 ± 6.22 ml•kg^{-1}•min^{-1} (95% CI: 31.65 – 43.49), 188.40 ± 4.52 bpm, with a respiratory exchange ratio of 1.25 ± 0.03 and perceived effort of 18.00 ± 1.41. Peak oxygen uptake for the males was insignificantly lower than cardiorespiratory fitness in a reference group of 191 men aged 20-29 who completed peak exercise on the cycle ergometer, $t(191)=1.38$, $p=.708$, $d=-0.32$ [43].

There was valid accelerometer data for seven participants. The group walked 6,342 ± 1,414 steps per day and completed 44.75 ± 15.26 minutes of moderate-to-vigorous physical activity (MVPA) per valid day. The sub-set of four women completed 44.29 ± 8.87 minutes/day of MVPA (95% CI: 35.89 – 52.69). MVPA for these females was significantly higher compared to a reference group of 219 females aged 20-29, $t(221)=2.53$, $p=.012$, $d=1.58$ [31]. The three males completed 45.37 ± 23.79 minutes/day of MVPA (95% CI: 18.45 – 72.28). MVPA for the males was insignificantly higher compared to a reference group of 212 males aged 20-29, $t(213)=0.33$, $p=.738$, $d=0.21$ [31].

Physical activity level was also assessed with a self-reported measure of past year physical activity. On average, participants reported a total of 358.30 ± 180.08 exercise units. The most common physical activities that this sample participated in during the past year included walking ($n=9$), running ($n=7$), and cycling ($n=7$). Females had a total of 385.00 ± 173.22 exercise units (95% CI: 256.68 – 513.32). This was insignificantly fewer exercise units compared to a reference group of 1,110 females aged 18-30, $t(1115)=0.21$, p=.837, $d=-0.09$ [33]. Males had a total of 296.00 ± 218.17 exercise units (95% CI: 49.12 – 542.88). This was insignificantly fewer exercise units compared to a reference group of 967 males aged 18-30, $t(968)=1.26$, $p=.208$, $d=-0.83$ [33].

3.4.4 Exercise vs. Rest

Submaximal exercise did not produce any obvious seizures.

Mood

Descriptive mood data for female and male sub-samples at each time point are presented in Table 3.5. For the full sample of 10 participants, no significant interactions were found for the tension, depression, anger, fatigue, or confusion subscales. For vigor, the condition x time interaction was significant, $F(2,32) = 4.21$, p=.024, η^2=.208. Post-hoc tests showed that, compared to baseline, vigor insignificantly increased immediately following exercise, $t(19)$=1.118, p=.227), and significantly decreased immediately following the rest condition, $t(19)$=2.23, p=.037). The combination resulted in a significant difference between the two conditions of 3.5 units immediately after exercise, $t(19)$=2.37, p=.0310, d=0.94. Analyses conducted without inclusion of covariates (treatment order and baseline mood scores) showed similar results. Group and individual vigor data are illustrated in Figures 3.2 and 3.3 respectively.

Wisconsin Cart Sorting Task

Descriptive Wisconsin Card Sort Task performance data are presented in Table 3.6. Raw errors and adjusted errors, after converting scores to the original 124-card version of the test, were stable across time in the exercise condition and insignificantly higher at the pre-test for the rest condition. The interactions for the error variables were insignificant. Response time was reduced immediately after rest and increased immediately after exercise; however, these changes did not result in a significant interaction. Analyses conducted without inclusion of covariates (treatment order and baseline WCST performance scores) showed similar results.

3.5 DISCUSSION

Much of the research examining the influence of exercise in people with epilepsy has focused on seizure control in humans and rodents [21]. Less attention has been paid to the possible psychological benefits of exercise, though increasingly, practitioners and researchers have called attention to the need for more research on the topics addressed in the present investigation [44]. The primary findings were that acute exercise transiently improved feelings of energy, but had no effect on attentional set shifting.

3.5.1 Exercise vs. Rest

Mood

Immediately following exercise, the participants reported feeling significantly more energetic compared to after seated rest. This benefit stemmed from a small increase in vigor after exercise and a small decrease in vigor following seated rest. This pattern is consistent with findings from one qualitative study involving detailed interviews with people with epilepsy [45] and quantitative studies exploring the mood effects of an acute bout of exercise in people without epilepsy [22]. A meta-analysis of 16 studies involving 678 individuals without epilepsy who completed acute exercise that was similar (typically cycling mode, moderate intensity, and between 20 and 40 minutes in duration) found that mean vigor t-scores were increased after exercise (53.3 to 57.9) and decreased (53.4 to 51.2) after the control conditions (typically quiet rest or lecture) [22]. More recent studies in people without epilepsy have confirmed that even short bouts (5 to 10 minutes) of exercise transiently improve feelings of energy compared to sitting, which produces feelings of low energy [46], and that changes of the magnitude observed in the present study exceed the energizing effect of the amount of caffeine contained in a 12-ounce can of soda [47]. Only one known study has evaluated changes in mood states following exercise in people with epilepsy, and it showed that POMS vigor scores significantly increased following a 12-week exercise program [48].

With increases in vigor, reductions in fatigue scores are plausible, but that did not occur for the present sample. In studies exploring mood effects of acute bouts of exercise in people without epilepsy, however, reductions in fatigue have been inconsistent [22]. Thus, it was not surprising that this sample showed insignificantly changed fatigue scores immediately following the cycling exercise. It is known that initial values can influence mood responses to acute exercise; therefore, low baseline fatigue scores prior to exercise may have limited the extent to which fatigue scores could be reduced after exercise. The present sample of females with epilepsy had significantly less vigor at baseline for the rest condition only, compared to a reference group of college aged adults [49]. Thus, the baseline values for vigor were consistent with previous findings that people with epilepsy experience less vigor than healthy comparison groups when measured by the POMS [6, 50, 51].

The other negative mood states measured by the POMS (tension, depression, anger, and confusion) also were not influenced by a single bout of exercise. The generally low baseline scores on these negative mood sates, compared to the norms, indicate that the sample was not suffering from negative affect (i.e., elevated anxiety and depression) of the type that can be common among people with epilepsy [5]. And although the sample reported lower than average general health, their perceptions of other aspects of physical and mental health assessed by the SF-36 were similar to normative samples of people without epilepsy. Logistics (e.g., conducting the study in a city without a large population) prevented the recruitment of a large sample of people with epilepsy, or targeting those with psychological distress who might have responded more positively to a single bout of exercise because of elevated symptoms at baseline.

Wisconsin Card Sorting Task

The present study showed that this sample of people with epilepsy committed significantly more perseveration errors on the Wisconsin Card Sorting Task at baseline for both exercise and rest conditions when compared to a reference group of similarly-aged adults [52]. This finding is consistent with previous evidence showing that people with epilepsy are at an increased risk for cognitive impairment, and experience some executive dysfunction as measured by the Wisconsin Card Sorting Task [53].

This study showed insignificant changes in response time and raw perseveration errors in Wisconsin Card Sort Task performance in response to cycling exercise. The error response pattern was not altered after using a formula to convert the findings for comparison to the more commonly used original version of the task. Immediately following the rest condition, the participants performed somewhat better on perseveration errors (by making an average of 2 fewer errors). The genesis of this non-significant improvement in performance is uncertain and performance returned to baseline during the second post-condition measurement trial. Compared to similar seated rest conditions, prior studies often, though do not always, show that executive functioning usually improves after a single bout of exercise [25-27]. One study found that participants without epilepsy experienced reductions in WCST performance at a vigorous intensity, but no impairment at light and moderate exercise intensities [54]. Perhaps the intensity of the acute bout of cycling exercise in the present was too high to show improvements in executive functioning, and caused a decline in performance instead.

3.5.2 Cardiorespiratory Fitness

The present study showed that both the sample of females and males with epilepsy were insignificantly less fit compared to a reference group of similarly aged adults [43]. The size of the difference for the sample of females (d= 0.05), however, is suggestive of a meaningful difference that could have been significant with a larger sample size. Though cardiorespiratory fitness has rarely been measured in people with epilepsy, this finding is generally consistent with Vancini et al.'s 2015 finding that 20 participants with temporal lobe epilepsy were significantly less fit than age- and gender-matched controls, measured with a graded maximal exercise test on a cycle ergometer [6]. Though Vancini et al. do not report cardiorespiratory fitness by gender, his sample of people with temporal lobe epilepsy is significantly less fit than the present sample of males with epilepsy, but similarly fit compared to the present sample of females with epilepsy [6]. This may be explained by the Vancini et al. sample being older than the present sample (mean age=34.1 ± 12.2), or the sample consisting of a large proportion of females.

3.5.3 Physical Activity

The present study showed that this sample of females with epilepsy participated in significantly more MVPA, and this sample of males with epilepsy participated in insignificantly more MVPA compared to a reference group of similarly aged adults, when measured by accelerometer [31]. This finding is surprising, as previous literature shows that people with epilepsy are significantly less active that people without epilepsy though MVPA has only previously been measured by self-report in people with epilepsy [14].

This study showed that this sample of females with epilepsy were insignificantly less active, and this sample of males with epilepsy were insignificantly less active compared to a reference group of similarly aged adults when measured with the CARDIA physical activity history questionnaire [33]. This finding is consistent with previous studies which have shown that people with epilepsy are significantly less active than people without epilepsy when measured by self-report [14]. It is unclear how this sample of people with epilepsy compares to other samples of people with epilepsy, as physical activity has not been measured in samples with epilepsy with the CARDIA physical activity history questionnaire.

3.5.4 Quality of Life

This study showed that health-related quality of life in this sample of young adults with epilepsy was largely similar to quality of life in a normative sample of similarly-aged adults [39]. This sample with epilepsy only demonstrated significant impairment compared to norms in the general health domain of the SF-36 health questionnaire.

The literature indicates that people with epilepsy tend to experience worse quality of life compared to people without epilepsy in the general population. It appears as if this sample does not experience this same impairment, and even demonstrates less impairment than another sample of people with epilepsy. It is important to take into account, however, a number of factors that may also influence quality of life: age, number of comorbid conditions present, seizure type, seizure severity and frequency, and duration of seizure disorder. This sample was young and healthy with well-controlled seizures, which probably contributes to their minimal impairments in quality of life. Also, it is possible that people with epilepsy with substantially lower than average perceptions of health in multiple domains are less likely to participate in studies involving vigorous exercise.

3.5.5 Limitations

Despite the wealth of new information gleaned from this investigation, it is not without its limitations. The most obvious limitation of this study is its small sample size, limiting its power to detect changes in psychological variables in response to acute exercise. Improvements in mood may have been difficult to detect due to this sample's low mood disturbance at baseline. This investigation also used an online version of the WCST, and it is unclear how sensitive this version may be to small changes in executive function. It is also difficult to compare performance on this version of the WCST to that of normative groups.

3.5.6 Conclusion

This investigation presents novel results regarding psychological responses to an acute bout of moderate-intensity exercise in people with epilepsy, as well as novel information about cardiorespiratory fitness and objectively measured physical activity levels in people with epilepsy. The present study demonstrates that acute exercise results in transient increases in feelings of energy without altering executive functioning in young adults with epilepsy. This study also found that this sample of young adults with epilepsy was similarly physically fit compared to a reference group of adults aged 20-29, and they completed similar amounts of MVPA when measured both objectively with accelerometry as well as with self-report. These finding should be interpreted with caution, as the study was not adequately powered to detect differences between this sample and comparison groups.

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Figure Captions

Figure 3.1: Screen shot of Wisconsin Card Sorting Task

Figure 3.2: Mean and SE vigor scores in the rest and exercise conditions across time

Figure 3.3: Individual vigor change scores for the rest and exercise conditions. Pre-scores were subtracted from immediate post-scores; thus, positive numbers reflect post-condition increases in vigor.

Table 3.1
Timing of Testing Procedures

Time (hours:min)	Task	Test Phase
Day 1		
0:00-0:02	Greet participant	Practice
0:02-0:10	Participant completes informed consent	Practice
0:10-0:20	Participant complete physical activity history questionnaire	Practice
0:20-0:25	Participant completes SF-36	Practice
0:25-0:30	Participant completes comorbidity questionnaire	Practice
0:30-0:40	Explain and practice Wisconsin Card Sort Task	Practice
0:40-0:50	Check performance and repeat practice trials if necessary	Practice
0:50-1:10	Perform maximal exercise test	Practice
1:10-1:15	Issue accelerometer and instructions	Practice
1:15-1:20	Schedule next visit	Practice
Days 2&3		
0:00-0:02	Greet participant	Baseline
0:02-0:04	Participant returns accelerometer	Baseline
0:07-0:12	Participant completes Profile of Mood States	Baseline
0:12-0:22	Participant completes Wisconsin Card Sort Task	Baseline
0:22-0:42	Experimental condition (20 min seated rest or 20 min cycling)	Treatment
0:42-0:47	Participant completes Profile of Mood States	Post-Treatment 1
0:47-0:57	Participant completes Wisconsin Card Sort Task	Post-Treatment 1
0:57-1:02	Break	Break
1:07-1:12	Participant completes Profile of Mood States	Post-Treatment 2
1:12-1:22	Participant completes Wisconsin Card Sort Task	Post-Treatment 2

Table 3.2
Participant demographics and epilepsy history (n=10)

	Mean	SD	Range
Age (yrs)	20.50	1.78	19.00 - 24.00
Height (cm)	171.40	7.58	157.00 - 187.00
Weight (kg)	61.03	9.38	49.00 - 80.00
BMI (kg/m^2)	20.81	3.23	16.73 - 28.01
Time Since First Seizure (yrs)	7.10	3.00	3.00 - 12.00
Time Since Last Seizure (yrs)	3.10	2.56	1.00 - 8.00
Seizures per Month	0.56	1.13	0.00 - 3.00

BMI = body mass index

Table 3.3
SF-36 Health Survey scores (n=10)

	Epilepsy (n=10)			Norms (n=173)[1]		
Domain	Mean	SD	95% CI	Mean	SD	Cohen's d
Physical Functioning	97.00	4.83	94.01 – 99.99	92.13	18.34	0.36
Role Physical	77.50	21.89	63.93 – 91.07	89.14	26.81	-0.48
Role Emotional	86.67	32.20	66.71 – 106.63	83.00	31.12	0.12
Vitality	54.00	14.30	45.14 – 62.86	62.53	19.58	-0.50
Mental Health	72.40	15.83	62.59 – 82.21	74.73	18.09	-0.14
Social Functioning	88.25	14.05	79.54 – 96.96	83.88	20.64	0.25
Bodily Pain	81.25	10.02	75.04 – 87.46	80.82	21.33	0.03
General Health	59.58	22.57	45.59 – 73.57	76.71	18.22	-0.83*

[1]Norms from [39].

*Present sample significantly lower (worse) compared to norms ($p<.05$)

Table 3.4

Fitness and physical activity

		Male Epilepsy n=2		Female Epilepsy n=5		Male Norms n=191[1]			Female Norms n=235[1]		
Fitness		Mean	SD	Mean	SD	Mean	SD	Cohens d	Mean	SD	Cohens d
	Test Duration (secs)	645.50	306.18	436.40	110.00						
	Peak RPE	18.00	1.41	15.00	2.45						
	Peak Leg Pain	9.00	1.41	4.80	3.03						
	Peak METs	11.20	1.84	7.80	0.99						
	Peak Power Output	187.50	53.03	145.00	27.39	288.00	61.00	-1.76*	173.00	46.00	-0.74
	Peak HR	188.00	4.24	181.40	5.55	180.00	17.50	0.63	178.00	14.40	0.31
	Peak RER	1.25	0.03	1.20	0.05	1.24	0.10	0.14	1.20	0.10	0.00
	Peak VO^2	39.20	6.22	27.26	3.52	42.00	10.50	-0.32	30.80	9.40	-0.50
		Male Epilepsy n=3		Female Epilepsy n=7		Male Norms n=967[2]			Female Norms n=1110[2]		
Physical Activity		Mean	SD	Mean	SD	Mean	SD	Cohens d	Mean	SD	Cohens d
Self-Report	CARDIA Vig. EU	163.00	158.92	226.57	128.99						
	CARDIA Mod. EU	133.00	116.12	158.43	118.79						
	CARDIA Total EU	296.00	218.17	385.00	173.22	513.70	299.20	-0.83	405.40	261.30	-0.09
		n=3		n=4		n=212[3]			n=219[3]		
Accelerometer	Steps/Day	5846.50	1936.67	6714.56	1034.06						
	Light PA (min/day)	747.44	33.66	821.21	85.07						
	Moderate PA (min/day)	36.73	11.24	41.83	7.02	37.90	27.66	-0.06	22.40	14.80	1.68*
	Vigorous PA (min/day)	7.24	10.63	1.79	2.49	1.90	4.37	0.65*	1.30	4.44	0.13
	MVPA (min/day)	45.37	23.79	44.29	8.87	39.70	29.12	0.21	23.60	16.28	1.58*

[1]Norms from [43]

[2]Norms from [33]

[3]Norms from [31]

*Present sample significantly different compared to norms (p<.05)

RPE = ratings of perceived exertion; MET = metabolic equivalent; HR = heart rate; RER = respiratory exchange ratio; VO^2 = oxygen uptake; EU = exercise units

Table 3.5
Profile of Mood States – Brief Form Scores

	Male Epilepsy (n=3)						Female Epilepsy (n=7)						Male Norms (n=63)			Female Norms (n=63)		
	Baseline		Post 1		Post 2		Baseline		Post 1		Post 2							
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	d	Mean	SD	d
Rest																		
Tension	4.67	5.69	2.67	4.62	3.00	4.36	1.14	1.21	0.14	0.38	0.43	0.79	6.40	3.70	-0.36	4.30	3.90	-1.09*
Depression	2.00	1.73	1.67	1.15	1.00	1.73	1.14	1.77	0.71	1.50	0.57	1.51	4.00	4.10	-0.64	2.50	3.50	-0.49
Anger	0.33	0.58	1.00	1.73	1.00	1.73	0.29	0.76	0.14	0.38	0.00	0.00	4.50	4.40	-1.33	2.60	3.40	-0.94
Vigor	5.00	2.65	1.33	1.15	2.33	2.52	6.57	4.43	5.14	3.39	4.43	3.46	11.60	4.20	-1.88*	11.00	5.50	-0.89*
Fatigue	3.00	4.36	5.00	6.08	4.67	6.35	7.86	1.95	4.29	2.70	4.86	3.02	7.40	4.40	-1.00	7.20	5.30	0.17
Confusion	3.00	1.00	1.67	1.15	2.00	1.00	3.29	1.8	2.43	2.07	1.86	1.95	5.00	3.30	-0.82	4.00	3.10	-0.28
Exercise																		
Tension	1.00	1.00	2.00	2.00	1.33	0.58	2.43	2.88	1.57	1.27	1.71	2.21	6.40	3.7	-1.99*	4.30	3.90	-0.55
Depression	0.33	0.58	0.33	0.58	0.00	0.00	1.14	1.86	0.57	1.51	0.57	1.51	4.00	4.1	-1.25	2.50	3.50	-0.49
Anger	0.00	0.00	0.00	0.00	0.33	0.58	0.71	0.76	0.29	0.49	0.00	0.00	4.50	4.4	-1.45	2.60	3.40	-0.77
Vigor	7.00	5.00	5.33	2.31	3.00	3.00	6.29	3.64	8.43	3.82	5.43	1.62	11.60	4.2	-1.00	11.00	5.50	-1.01*
Fatigue	3.67	3.79	8.00	1.73	6.33	1.15	4.71	1.8	4.57	1.13	3.86	1.35	7.40	4.4	-0.91	7.20	5.30	-0.63
Confusion	2.00	1.00	1.00	0.00	0.67	1.15	2.57	1.81	1.86	1.68	2.00	1.63	5.00	3.3	-1.23	4.00	3.10	-0.56

[1]Norms from [47]
*Present sample significantly different at baseline compared to norms (p<.05)

Table 3.6

Wisconsin Card Sorting Task Scores

	Baseline		Post 1		Post 2		Norms (n=1362)[1]		Cohen's d
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Rest									
Response Time (Correct)	1646.41	289.52	1578.34	244.14	1580.67	339.77			
Perseveration Errors (Raw)	7.30	2.00	5.20	1.14	6.80	2.49			
Perseveration Errors (Converted)	13.33	3.37	9.39	1.75	12.39	4.29	6.92	5.04	1.50*
Exercise									
Response Time (Correct)	1695.98	404.23	1818.06	524.06	1660.49	451.99			
Perseveration Errors (Raw)	6.20	2.62	6.30	1.06	6.20	2.49			
Perseveration Errors (Converted)	11.27	4.53	11.45	1.60	11.27	4.29	6.92	5.04	0.91*

[1]Norms from [50]

*Present sample significantly different from norms at baseline ($p<.05$)

Figure 3.1

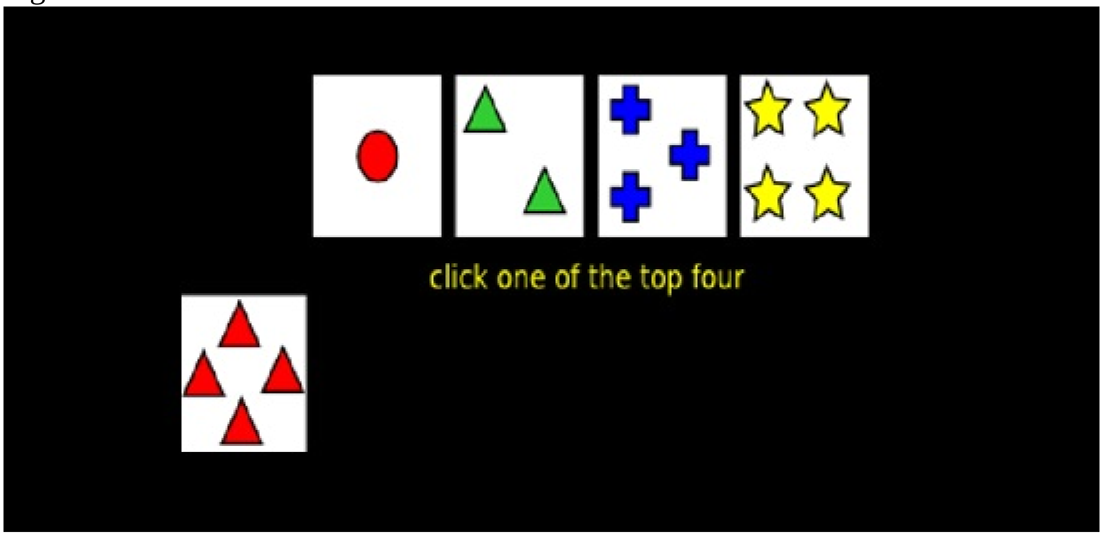


Figure 3.2

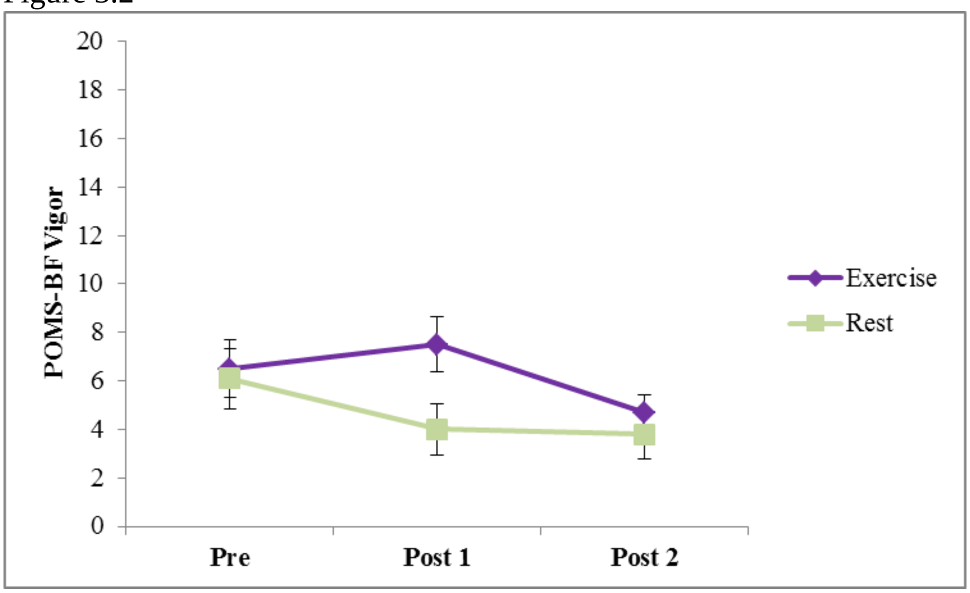
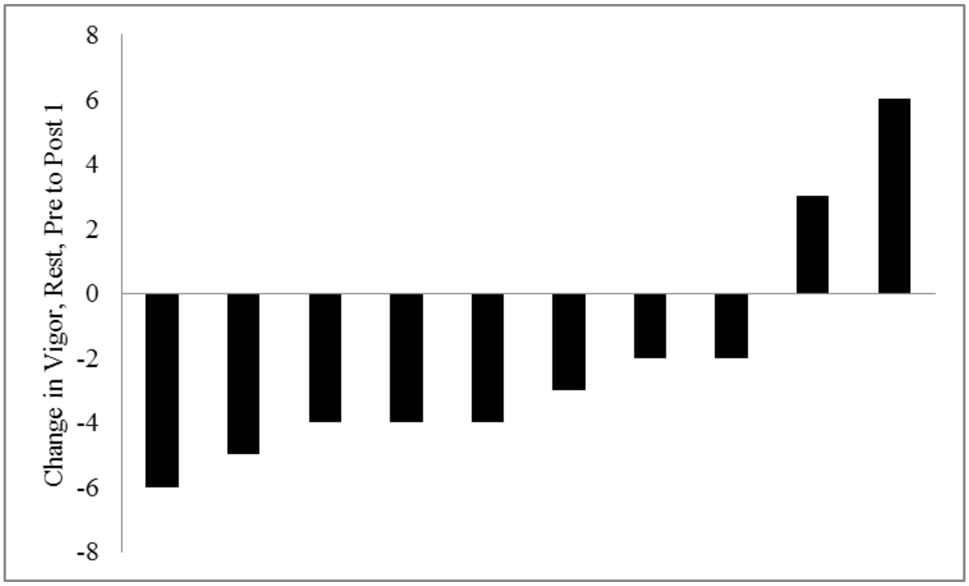
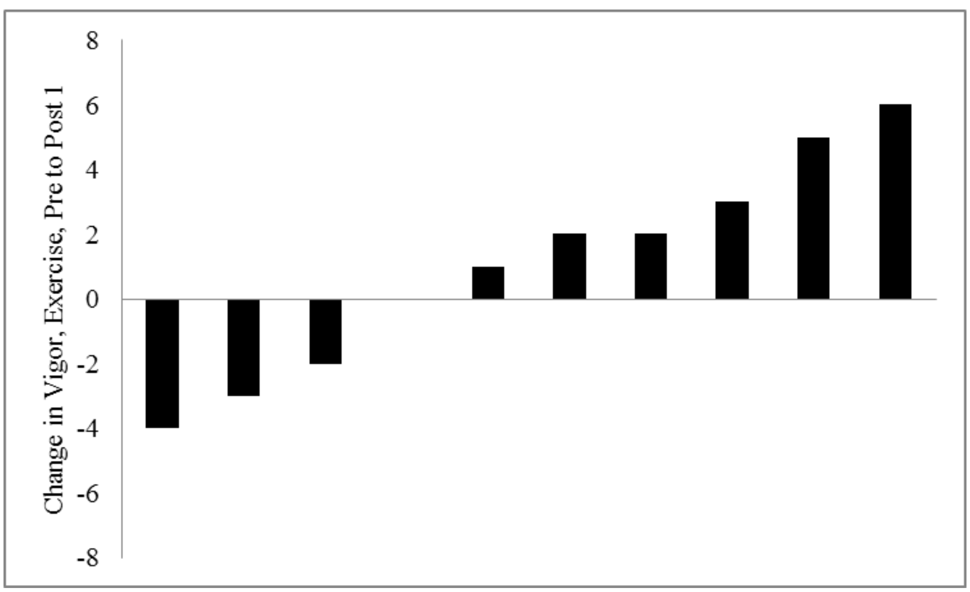


Figure 3.3

Rest



Exercise



APPENDICES

A. Physical Activity Readiness Questionnaire

Physical Activity Readiness Questionnaire (PAR-Q)		
Date:		**Participant ID:**
Please read the statements carefully and answer each one honestly: check YES or NO.		
Yes	**No**	
		1. I have a heart condition and my healthcare professional recommends only medically supervised physical activity.
		2. During or right after I exercises, I often have pains or pressure in my neck, left shoulder, or arm.
		3. I have developed chest pain within the last month.
		4. I tend to lose consciousness or fall over sure to dizziness.
		5. I feel extremely breathless after mild exertion.
		6. My healthcare provider recommended that I take medicine for high blood pressure or a heart condition.
		7. I have a bone or joint problems that limit my ability to do moderate-intensity physical activity.
		8. I have a medical condition or other physical reason not mentioned here that might need special attention in an exercise program.

B. Demographic and Epilepsy History Questionnaire

Participant ID:_______________ Date: ______________

Sex:________________________ Age:_______________

1. **Have you been diagnosed with epilepsy by a doctor?**

   Yes No

2. **Etiology of seizures**

   a. Genetic b. Brain Structure c. Brain Metabolism

   d. Unknown e. Other______________________________________

3. **Specific Etiology**

   a. Traumatic Brain Injury b. Chromosomal Disorder c. Meningitis

   d. Encephalitis e. Mitochondrial Disorder f. Stroke

   g. Error in brain development h. Metabolic Disorder i. Tumor

   j. Unknown k. other________________________________

4. **Date of First Seizure**

5. **Date of Last Seizure**

6. **How often do you have seizures?**

   ________________________x/month

7. **Can you tell if you are about to have a seizure? If yes, please explain briefly.**

8. **Are you taking medication for seizures?**

Yes No

Medication	Dosage	Times/Day	Medication	Dosage	Times/Day

9. **If you have any side effects to seizure medications, please explain**

10. **Is there anything else that you think we should know about your seizures?**

C. CARDIA Physical Activity History Questionnaire

This questionnaire will ask you about some specific activities and the amount of time you spend doing each. Only include time spend actually doing the activity. For example, sitting by the pool does not count as time swimming; sitting in a chair lift does not count as time skiing.
First, you will be asked about vigorous activities. Vigorous activities increase your heart rate or make you sweat when doing them or make you breathe hard or raise your body temperature. If you do an activity, but not vigorously, please include it later when you are asked about other non-strenuous sports.

The first vigorous activity is running or jogging. Did you run or jog in the past 12 months for at least one hour total time in any month? For instance, you might have done three 20-minute sessions in the month. (Vigorous backpacking, hiking, or mountain climbing may also be included)

___ Yes →	2. How many months did you do this activity?	________
___ No ↓	3. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	4. (How many of these months/In this month) did you do this activity for at least **2** hours a week?	________

Did you do vigorous raquet sports in the past 12 months for at least one hour total time in any month? For instance, you might have done three 20-minute sessions in the month. (Tennis, Badminton, Paddle ball, racquetball, handball, squash)

___ Yes →	6. How many months did you do this activity?	________
___ No ↓	7. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	8. (How many of these months/In this month) did you do this activity for at least **3** hours a week?	________

Did you bicycle faster than 10 miles an hour or exercise hard on an exercise bicycle in the past 12 months for at least one hour total time in any month? (Vigorous exercise on a rowing machine may also be included).

___ Yes →	10. How many months did you do this activity?	________
___ No ↓	11. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	12. (How many of these months/In this month) did you do this activity for at least **2** hours a week?	________

Did you swim in the past 12 months for at least one hour in total time in any month? (Snorkeling and scuba diving may also be included)

___ Yes →	14. How many months did you do this activity?	________
___ No ↓	15. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	16. (How many of these months/In this month) did you do this activity for at least **2** hours a week?	________

Did you do a vigorous exercise class or vigorous dancing in the past 12 months for at least one hour total time in any month? (Jazzercise, Jane Fonda-type workout, aerobic dancing, and ballet may be included)

___ Yes →	18. How many months did you do this activity?	________
___ No ↓	19. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	20. (How many of these months/In this month) did you do this activity for at least **3** hours a week?	________

Did you do a vigorous job activity such as lifting, carrying, or digging in the past 12 months for at least one hour total time in any month? (Loading trucks and stacking lumber may be included)

___ Yes →	22. How many months did you do this activity?	________
___ No ↓	23. (How many of these months/In this month) did you do this activity for at least **2** hour a week?	________
	24. (How many of these months/In this month) did you do this activity for at least **5** hours a week?	________

Did you do home or leisure activity such as snow shoveling, moving heavy objects, or weight lifting in the past 12 months for at least one hour total time in any month? (Shoveling sand or gravel, a nautilus workout, or moving furniture may be included)

___ Yes →	26. How many months did you do this activity?	________
___ No ↓	27. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	28. (How many of these months/In this month) did you do this activity for at least **3** hours a week?	________

Did you do any other strenuous sports such as basketball, football, skating, or skiing in the past 12 months for at least one hour total time in any month? (Martial arts, soccer, rugby, land or water skiing, ice or roller skating may be included.)

___ Yes →	30. How many months did you do this activity?	________
___ No ↓	31. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	32. (How many of these months/In this month) did you do this activity for at least **3** hours a week?	________

Now, you will be asked about more leisurely activities.

Did you do nonstrenuous sports such as softball, shooting baskets, volleyball, ping pong, leisurely jogging, swimming, or biking which was not included before in the past 12 months for at least one hour total time in any month? (Horseback riding, fishing from bank or boat, archery, non-vigorous rowing or sailing, and non-vigorous biking may be included)

___ Yes ➔	34. How many months did you do this activity?	______
___ No 🡻	35. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	______
	36. (How many of these months/In this month) did you do this activity for at least **3** hours a week?	______

Did you take walks or hikes or walk to work in the past 12 months for at least one hour total time in any month? (Stream fishing or hunting may be included.)

___ Yes ➔	38. How many months did you do this activity?	______
___ No 🡻	39. (How many of these months/In this month) did you do this activity for at least **2** hour a week?	______
	40. (How many of these months/In this month) did you do this activity for at least **4** hours a week?	______

Did you bowl or play golf in the past 12 months for at least one hour total time in any month?

___ Yes ➔	42. How many months did you do this activity?	______
___ No 🡻	43. (How many of these months/In this month) did you do this activity for at least **1** hour a week? ____ Always use motorized cart	______
	44. (How many of these months/In this month) did you do this activity for at least **3** hours a week? ____ Always use motorized cart	______

Did you do home exercises or calisthenics in the past 12 months for at least one hour total time in any month? (Non-vigorous exercise or rowing machine may be included)

___ Yes ➔	46. How many months did you do this activity?	________
___ No ➔	47. (How many of these months/In this month) did you do this activity for at least **1** hour a week?	________
	48. (How many of these months/In this month) did you do this activity for at least **3** hours a week?	________

Did you do home maintenance and gardening, including carpentry, painting, raking, and mowing in the past 12 months for at least one hour total time in any month? (Hanging wallpaper, weeding, and gardening may be included).

___ Yes ➔	50. How many months did you do this activity?	________
___ No ➔	51. (How many of these months/In this month) did you do this activity for at least **2** hour a week?	________
	52. (How many of these months/In this month) did you do this activity for at least **5** hours a week?	________

List sports or other activities not elsewhere classified

SPORT:____

54. Have you already counted this in any other category?

___ Yes (if yes, do not record here) ___ No

55. How many months? _____ 56. Average hrs. in those months? _____

57. List sports or other activities not elsewhere classified

D. Profile of Mood States – Brief Form

POMS Brief Form					
Participant ID:		**Age:**		**Gender:**	
Birth Date:		**Today's Date:**			
Below is a list of words that describe feelings that people have. Please read each word carefully. Then circle the number that best describes how you feel **RIGHT NOW**.					
	Not at all	**A Little**	**Moderately**	**Quite a bit**	**Extremely**
1. Tense	0	1	2	3	4
2. Angry	0	1	2	3	4
3. Worn Out	0	1	2	3	4
4. Lively	0	1	2	3	4
5. Confused	0	1	2	3	4
6. Shaky	0	1	2	3	4
7. Sad	0	1	2	3	4
8. Active	0	1	2	3	4
9. Grouchy	0	1	2	3	4
10. Energetic	0	1	2	3	4
11. Unworthy	0	1	2	3	4
12. Uneasy	0	1	2	3	4
13. Fatigued	0	1	2	3	4
14. Annoyed	0	1	2	3	4
15. Discouraged	0	1	2	3	4
16. Nervous	0	1	2	3	4
17. Lonely	0	1	2	3	4
18. Muddled	0	1	2	3	4
19. Exhausted	0	1	2	3	4
20. Anxious	0	1	2	3	4
21. Gloomy	0	1	2	3	4
22. Sluggish	0	1	2	3	4
23. Weary	0	1	2	3	4
24. Bewildered	0	1	2	3	4
25. Furious	0	1	2	3	4
26. Efficient	0	1	2	3	4
27. Full of pep	0	1	2	3	4
28. Bad-tempered	0	1	2	3	4
29. Forgetful	0	1	2	3	4
30. Vigorous	0	1	2	3	4

E. SF-36 Health Survey

ID #________________ **Date______________**

INSTRUCTIONS:

This survey asks for your views about your health. This information will be summarized in your medical record and will help your doctors keep track of how you feel and how well you are able to do your usual activities.

Answer every question by circling the appropriate number, 1, 2, 3, … If you are unsure about how to answer a question, please give the best answer you can and make a comment in the left margin.

1. **In general, would you say your health is:**

(circle one number)

Excellent………..……………………………..1
Very good………………………………………2
Good……………………………………………3
Fair……………………………………………..4
Poor…………………………………………….5

2. **Compared to one year ago, how would you rate your health in general now?**

(circle one number)

Much better now than one year ago……………1
Somewhat better now than one year ago………2
About the same………………………………..3
Somewhat worse now than one year ago………4
Much worse now than one year ago……………5

HEALTH AND DAILY ACTIVITIES

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (Circle 1, 2, or 3 on each line).

	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. Moderate activities, such as moving a Table, pushing a vacuum cleaner, Bowling, or playing golf	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing several flights of stairs	1	2	3
e. Climbing one flight of stairs	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking more than a mile	1	2	3
h. Walking several blocks	1	2	3
i. Walking one block	1	2	3
j. Bathing and dressing yourself	1	2	3

4. **During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health</u>? (Please answer <u>YES</u> or <u>NO</u> for each question by circling 1 or 2 on each line).**

	YES	**NO**
a. Cut down on the amount of time you spent on work or other activities	**1**	**2**
b. Accomplished less than you would like	**1**	**2**
c. Were limited in the kind of work or other activities	**1**	**2**
d. Had difficulty performing the work or other activities (for example, it took extra effort)	**1**	**2**

5. **During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious?)**
(Please answer <u>YES</u> or <u>NO</u> for each question by circling 1 or 2 on each line).

	YES	**NO**
a. Cut down the amount of time you spent on work or other activities	**1**	**2**
b. Accomplished less than you would like	**1**	**2**
c. Didn't do work or other activities as carefully as usual	**1**	**2**

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(circle one number)

Not at all……………………………………1
Slightly…………………………………...2
Moderately………………………………3
Quite a bit……………………………….4
Extremely………………………………..5

PAIN

7. How much bodily pain have you had during the past 4 weeks?

(circle one number)

None……………………………………...1
Very mild……………………………….. .2
Mild………………………………………3
Moderate………………………………...4
Severe……………………………………5
Very severe……………………………...6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one number)

Not at all……………………………………1
A little bit……………………………….. .2
Moderately………………………………3
Quite a bit……………………………….4
Extremely………………………………..5

YOUR FEELINGS

9. These questions are about how you feel and how things have been with you <u>during the past month</u>. For each question, please indicate the one answer that comes closest to the way you have been feeling.

How much of the time during the <u>past month</u>…

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
a. did you feel full of pep?	1	2	3	4	5	6
b. have you been a very nervous person?	1	2	3	4	5	6
c. have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. have you felt calm and peaceful?	1	2	3	4	5	6
e. did you have a lot of energy?	1	2	3	4	5	6
f. have you felt downhearted and blue?	1	2	3	4	5	6
g. did you feel worn out?	1	2	3	4	5	6
h. have you been a happy person?	1	2	3	4	5	6
i. did you feel tired?	1	2	3	4	5	6
j. has your <u>health limited your social activities</u> (like visiting with friends or close relatives)?	1	2	3	4	5	6

HEALTH IN GENERAL

10. Please choose the answer that best describes how true or false each of the following statements is for you.

(circle one number on each line)

	Definitely True	Mostly True	Not Sure	Mostly False	Definitely False
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

F. Self-Administered Comorbidity Questionnaire

The following is a list of common problems. Please indicate if you currently have the problem in the first column. If you do not have the problem, skip to the next problem.
If you do have the problem, please indicate in the second column if you receive medications or some other type of treatment for this problem.
In the third column, indicate if the problem limits any of your activities.
Finally, indicate all medical conditions that are not listed under "other medical problems" at the end of the page.

PROBLEM	**Do you have the problem?**		**Do you receive treatment for it?**		**Does it limit your activities?**	
	No	**Yes →**	**No**	**Yes**	**No**	**Yes**
Heart Disease	N	Y	N	Y	N	Y
High Blood Pressure	N	Y	N	Y	N	Y
Lung Disease	N	Y	N	Y	N	Y
Diabetes	N	Y	N	Y	N	Y
Ulcer or stomach disease	N	Y	N	Y	N	Y
Kidney Disease	N	Y	N	Y	N	Y
Liver Disease	N	Y	N	Y	N	Y
Anemia or other blood disease	N	Y	N	Y	N	Y
Cancer	N	Y	N	Y	N	Y
Depression	N	Y	N	Y	N	Y
Osteoarthritis, degenerative arthritis	N	Y	N	Y	N	Y
Back pain	N	Y	N	Y	N	Y
Rheumatoid arthritis	N	Y	N	Y	N	Y
Other medical problems (please write in)						
	N	Y	N	Y	N	Y
	N	Y	N	Y	N	Y