Effects of Cardiovascular Exercise on Cognitive Function in Individuals with Parkinson’s Disease

A thesis submitted in partial fulfillment of the requirements For the degree of Masters of Science in Kinesiology

By

Jessica McCamish

May 2013
This thesis of Jessica Elise McCamish is approved:

_________________________________________  ______________
Ashley Samson, Ph.D.  Date

_________________________________________  ______________
Konstantinos Vrontistinos, Ph.D.  Date

_________________________________________  ______________
Taeyou Jung, Ph.D., ATC, CAPE, Chair  Date

California State University, Northridge
DEDICATION

This work is dedicated to my Lord and Savior for without Him none of my work could have been done. Isaiah 40:31 – “But those who hope in the Lord will renew their strength. They will soar on wings like eagles; they will run and not grow weary, they will walk and not be faint”.

This work is also dedicated to my parents. Mark and Barbara McCamish – thank you doesn’t cover the dedication, support, and love you have given me not just through these past 2 years but through my whole life. I am truly blessed to have you as my parents.
I would like to acknowledge my thesis advisor, Dr. Taeyou Jung, for all of his help and support. To Dr. Samson, thank you for all of the times you met with me, helped me sort through all of my data, and the encouragement you provided before each of my presentations. To Dino, thank you for your encouragement and confidence in my abilities, you made this process fun and exciting.

Thank you to all of my colleagues and friends at the Center of Achievement for your help; from running intervention sessions to reviewing presentations. I would not have been successful without the efforts of these people: Gioella, Byron, Cameron and Leora. To Mai; thank you for meeting with me, sharing your knowledge and your experience, and for letting me vent when I needed someone to talk to who has been there and understands. I feel so lucky to be able to not only know you as my instructor and mentor but also my friend. To Jen; thank you for your continued support and working with me during crunch time before all of my presentations. I will always cherish those ‘freak out’ moments in our freezing office or laughing until tears were pouring from our eyes due to lack of sleep. The past 2 years have truly been an amazing adventure friend!

To my family I consider an honor to be a part of, thank you for your love and support, the long phone calls, the prayers, and the laughter and fun you brought to my life during the immense stress of this process. I love you all so much!

To my best friend, Lauren, I cannot express my appreciation for all you have done for me these past two years. I could not have gotten through this without your support and love. Thank you for all the dinners you cooked, the dishes you cleaned, the coffee you made, and for taking care of me when I was sick, and over tired. You sacrificed so much of yourself and your time for me and I am truly blessed to have you in my life. Thank you and I love you!
# TABLE OF CONTENTS

SIGNATURE PAGE .............................................. ii
DEDICATION ................................................... iii
ACKNOWLEDGEMENTS ....................................... iv
LIST OF TABLES ................................................ vii
LIST OF FIGURES ........................................... viii
ABSTRACT ...................................................... xi

INTRODUCTION ................................................ 1

LITERATURE REVIEW .......................................... 4

PARKINSON’S DISEASE ........................................ 4
PATHOLOGY ..................................................... 4
PD AND COGNITIVE FUNCTION .............................. 5
EXERCISE AND COGNITIVE FUNCTION .................... 6
EXERCISE AND PD ............................................ 9
EXERCISE AND COGNITIVE FUNCTION IN PD ............. 12
SUMMARY ....................................................... 13

METHODS ....................................................... 16

PARTICIPANTS .................................................. 16
SETTING AND DESIGN ......................................... 16
VARIABLES AND INSTRUMENTATION ......................... 17
INTERVENTION PROTOCOL .................................... 17
DATA COLLECTION PROCEDURES ............................ 18
STATISTICAL ANALYSIS ....................................... 19
HUMAN SUBJECTS PROTOCOL ................................ 19

RESULTS ......................................................... 20

PARTICIPANT #1 ............................................... 20
PARTICIPANT #2 ............................................... 28
PARTICIPANT #3 ............................................... 38
PARTICIPANT #4 ............................................... 46
PARTICIPANT #5 ............................................... 54
PARTICIPANT #6 ............................................... 61
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISCUSSION</td>
<td>86</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>86</td>
</tr>
<tr>
<td>CEG</td>
<td>86</td>
</tr>
<tr>
<td>HSG</td>
<td>88</td>
</tr>
<tr>
<td>GROUPS</td>
<td>89</td>
</tr>
<tr>
<td>ADHERENCE</td>
<td>89</td>
</tr>
<tr>
<td>LIMITATIONS</td>
<td>90</td>
</tr>
<tr>
<td>FUTURE RESEARCH</td>
<td>90</td>
</tr>
<tr>
<td>CONCLUSION</td>
<td>91</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>92</td>
</tr>
<tr>
<td>APPENDIX A – ADDITIONAL TABLES</td>
<td>94</td>
</tr>
<tr>
<td>APPENDIX B – ADDITIONAL FIGURE</td>
<td>96</td>
</tr>
<tr>
<td>APPENDIX C – CONSENT FORM</td>
<td>97</td>
</tr>
<tr>
<td>APPENDIX D – BILL OF RIGHTS</td>
<td>102</td>
</tr>
<tr>
<td>APPENDIX E – COPY OF SCOPA-COG</td>
<td>103</td>
</tr>
<tr>
<td>APPENDIX F – COPY OF PDQ-39</td>
<td>110</td>
</tr>
</tbody>
</table>
LIST OF TABLES

RESULTS SUMMARIES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td>Participant #1</td>
<td>27</td>
</tr>
<tr>
<td>Table 2</td>
<td>Participant #2</td>
<td>37</td>
</tr>
<tr>
<td>Table 3</td>
<td>Participant #3</td>
<td>45</td>
</tr>
<tr>
<td>Table 4</td>
<td>Participant #4</td>
<td>53</td>
</tr>
<tr>
<td>Table 5</td>
<td>Participant #5</td>
<td>60</td>
</tr>
<tr>
<td>Table 6</td>
<td>Participant #6</td>
<td>68</td>
</tr>
<tr>
<td>Table 7</td>
<td>Participant #7</td>
<td>76</td>
</tr>
<tr>
<td>Table 8</td>
<td>CEG &amp; HSG</td>
<td>85</td>
</tr>
<tr>
<td>Table 9</td>
<td>Age Demographics: Appendix A</td>
<td>94</td>
</tr>
<tr>
<td>Table 10</td>
<td>H&amp;Y Distribution: Appendix A</td>
<td>94</td>
</tr>
<tr>
<td>Table 11</td>
<td>Number and Percent Improvement, Decline, Maintain: Appendix A</td>
<td>95</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

## PARTICIPANT #1

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Verbal Memory</td>
<td>22</td>
</tr>
<tr>
<td>1B</td>
<td>Executive Function</td>
<td>22</td>
</tr>
<tr>
<td>1C</td>
<td>Psychomotor Speed</td>
<td>23</td>
</tr>
<tr>
<td>1D</td>
<td>Cognitive Flexibility</td>
<td>23</td>
</tr>
<tr>
<td>1E</td>
<td>Neurocognitive Index</td>
<td>24</td>
</tr>
<tr>
<td>1F</td>
<td>Reaction Time</td>
<td>24</td>
</tr>
<tr>
<td>1G</td>
<td>Visual Memory</td>
<td>25</td>
</tr>
<tr>
<td>1H</td>
<td>Verbal Recall</td>
<td>25</td>
</tr>
<tr>
<td>1I</td>
<td>Total Score</td>
<td>26</td>
</tr>
<tr>
<td>1J</td>
<td>Cognitive Impairment</td>
<td>26</td>
</tr>
<tr>
<td>1K</td>
<td>Single Index</td>
<td>27</td>
</tr>
</tbody>
</table>

## PARTICIPANT #2

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2A</td>
<td>Executive Function</td>
<td>30</td>
</tr>
<tr>
<td>2B</td>
<td>Psychomotor Speed</td>
<td>30</td>
</tr>
<tr>
<td>2C</td>
<td>Reaction Time</td>
<td>31</td>
</tr>
<tr>
<td>2D</td>
<td>Cognitive Flexibility</td>
<td>31</td>
</tr>
<tr>
<td>2E</td>
<td>Neurocognitive Index</td>
<td>32</td>
</tr>
<tr>
<td>2F</td>
<td>Verbal Memory</td>
<td>32</td>
</tr>
<tr>
<td>2G</td>
<td>Continuous Performance Test</td>
<td>33</td>
</tr>
<tr>
<td>2H</td>
<td>Semantic Fluency</td>
<td>33</td>
</tr>
<tr>
<td>2I</td>
<td>Delayed Recall</td>
<td>34</td>
</tr>
<tr>
<td>2J</td>
<td>Total Score</td>
<td>34</td>
</tr>
<tr>
<td>2K</td>
<td>Dice</td>
<td>35</td>
</tr>
<tr>
<td>2L</td>
<td>Digit Span Backward</td>
<td>35</td>
</tr>
<tr>
<td>2M</td>
<td>Cognitive Impairment</td>
<td>36</td>
</tr>
<tr>
<td>2N</td>
<td>Single Index</td>
<td>36</td>
</tr>
</tbody>
</table>

## PARTICIPANT #3

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3A</td>
<td>Verbal Memory</td>
<td>40</td>
</tr>
<tr>
<td>3B</td>
<td>Executive Function</td>
<td>40</td>
</tr>
<tr>
<td>3C</td>
<td>Complex Attention</td>
<td>41</td>
</tr>
<tr>
<td>3D</td>
<td>Cognitive Flexibility</td>
<td>41</td>
</tr>
<tr>
<td>3E</td>
<td>Processing Speed</td>
<td>42</td>
</tr>
<tr>
<td>3F</td>
<td>Neurocognitive Index</td>
<td>42</td>
</tr>
<tr>
<td>3G</td>
<td>Verbal Recall</td>
<td>43</td>
</tr>
<tr>
<td>3H</td>
<td>Dice</td>
<td>43</td>
</tr>
<tr>
<td>Figure 3I - Total Score</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Figure 3J - Single Index</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Figure 3K - Cognitive Impairment</td>
<td>45</td>
<td></td>
</tr>
</tbody>
</table>

**Participant #4**

| Figure 4A - Reaction Time | 48 |
| Figure 4B - Continuous Performance Test | 48 |
| Figure 4C - Complex Attention | 49 |
| Figure 4D - Neurocognitive Index | 49 |
| Figure 4E - Indicate Cubes | 50 |
| Figure 4F - Months Backwards | 50 |
| Figure 4G - Semantic Fluency | 51 |
| Figure 4H - Delayed Recall | 51 |
| Figure 4I - Total Score | 52 |
| Figure 4J - Single Index | 52 |
| Figure 4K - Cognitive Impairment | 53 |

**Participant #5**

| Figure 5A - Executive Function | 56 |
| Figure 5B - Complex Attention | 56 |
| Figure 5C - Cognitive Flexibility | 57 |
| Figure 5D - Reaction Time | 57 |
| Figure 5E - Neurocognitive Index | 58 |
| Figure 5F - Attention | 58 |
| Figure 5G - Total Score | 59 |
| Figure 5H - Single Index | 59 |
| Figure 5I - Cognitive Impairment | 60 |

**Participant #6**

| Figure 6A - Complex Attention | 63 |
| Figure 6B - Cognitive Flexibility | 63 |
| Figure 6C - Psychomotor Speed | 64 |
| Figure 6D - Neurocognitive Index | 64 |
| Figure 6E - Indicate Cubes | 65 |
| Figure 6F - Attention | 65 |
| Figure 6G - Fist-Edge-Palm | 66 |
| Figure 6H - Dice | 66 |
| Figure 6I - Total Score | 67 |
| Figure 6J - Cognitive Impairment | 67 |
| Figure 6K - Single Index | 68 |
### GROUP RESULTS

<table>
<thead>
<tr>
<th>Figure 8A</th>
<th>Executive Function</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 8B</td>
<td>Complex Attention</td>
<td>80</td>
</tr>
<tr>
<td>Figure 8C</td>
<td>Cognitive Flexibility</td>
<td>81</td>
</tr>
<tr>
<td>Figure 8D</td>
<td>Neurocognitive Index</td>
<td>81</td>
</tr>
<tr>
<td>Figure 8E</td>
<td>Verbal Recall</td>
<td>82</td>
</tr>
<tr>
<td>Figure 8F</td>
<td>Indicate Cubes</td>
<td>82</td>
</tr>
<tr>
<td>Figure 8G</td>
<td>Months Backwards</td>
<td>83</td>
</tr>
<tr>
<td>Figure 8H</td>
<td>Total Score</td>
<td>83</td>
</tr>
<tr>
<td>Figure 8I</td>
<td>Cognitive Impairment</td>
<td>84</td>
</tr>
<tr>
<td>Figure 8J</td>
<td>Single Index</td>
<td>84</td>
</tr>
</tbody>
</table>

### RECRUITMENT FLOW CHART: APPENDIX B

<table>
<thead>
<tr>
<th>Figure 7A</th>
<th>Reaction Time</th>
<th>71</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 7B</td>
<td>Continuous Performance Test</td>
<td>71</td>
</tr>
<tr>
<td>Figure 7C</td>
<td>Processing Speed</td>
<td>72</td>
</tr>
<tr>
<td>Figure 7D</td>
<td>Psychomotor Speed</td>
<td>72</td>
</tr>
<tr>
<td>Figure 7E</td>
<td>Neurocognitive Index</td>
<td>73</td>
</tr>
<tr>
<td>Figure 7F</td>
<td>Indicate Cubes</td>
<td>73</td>
</tr>
<tr>
<td>Figure 7G</td>
<td>Fist-Edge-Palm</td>
<td>74</td>
</tr>
<tr>
<td>Figure 7H</td>
<td>Delayed Recall</td>
<td>74</td>
</tr>
<tr>
<td>Figure 7I</td>
<td>Total Score</td>
<td>75</td>
</tr>
<tr>
<td>Figure 7J</td>
<td>Single Index</td>
<td>75</td>
</tr>
<tr>
<td>Figure 7K</td>
<td>Cognitive Impairment</td>
<td>76</td>
</tr>
</tbody>
</table>
ABSTRACT

The Effects of Aerobic Exercise on Cognitive Function in Individuals with Parkinson’s Disease

by

Jessica E. McCamish

Master of Science in Kinesiology

OBJECTIVE: To examine the effects of cardiovascular exercise (CVE) on cognitive function in individuals with Parkinson’s Disease (PD).

BACKGROUND: The effects of CVE on cognitive function have been well documented in the healthy aging population. Most previous studies involving exercise and PD have primarily examined motor outcomes, such as balance and gait. Few studies have examined the effectiveness of exercise, specifically CVE, on cognitive function in populations with PD.

METHODS: A total of 7 male participants (age 65± 3) with PD between the stages of one and three on the Hoehn & Yahr stage of severity (H&Y) were randomly assigned to the cardiovascular exercise group (CEG) or home stretching group (HSG). Each participant in the CEG performed 30-40 minutes of stationary bike exercise three times a week at 60 - 75% of the individual’s age-predicted maximum heart rate over a 12-week intervention period. The HSG was provided a home-based stretching manual and instructed to perform mild stretches at home three times per week for the same 12-week period. Cognitive tests were administered using the CNS Vital Signs © (CNSVS) cognitive function test battery and the Scales for Outcomes in Parkinson’s Disease – Cognition (SCOPA-cog) ©. In addition, quality of life (QoL) was assessed using the Parkinson’s Disease Questionnaire
All tests were administered four times: pre-intervention, 4-weeks and, 8-weeks during intervention, and post-intervention.

RESULTS: Visual analysis showed greater numerical improvements in: executive function (EF), complex attention, cognitive flexibility, and overall cognitive function among participants in the CEG as compared to those in the HSG. Those in the CEG also showed a greater numerical improvement in QoL and perceived cognitive impairment over individuals in the HSG.

CONCLUSION: The findings suggest that the study design is adequate to formally test the hypothesis regarding CVE impacting cognitive function in PD and that CVE may be helpful for people with PD to maintain and improve cognitive function and QoL.
INTRODUCTION

PD is a neurodegenerative disease that affects, on estimate more than one million individuals in the United States (Carne et al., 2005). PD occurs due to a necrosis of dopamine producing cells in the substantia nigra and reduce production of dopamine below normal levels and is characterized by physical manifestations such as: bradykinesia, rigidity, tremors at rest, compromised gait, impaired balance and coordination, and diminished vocal and physical expression (Baatile, Langbein, Weaver, Maloney, & Jost, 2000). The nature of this disease is a progressive deterioration of both physical and cognitive functions (McKeith, 2004; Sawle, 2004). The physical manifestations are typically used to identify the level of severity in individuals with PD using the H&Y scale, which ranges from the least severe level of one to the most severe level of five. Individuals with PD are often treated by pharmacological methods, such as a dopamine supplement as well as a surgical procedure known as deep brain stimulation (DBS) (McKeith, 2004; Shotbolt et al., 2011). These treatments are used to minimize the physical manifestations of PD. However, since PD is progressive, the amount of medicine increases over time as symptoms increase (McKeith, 2004).

While the physical symptoms are most recognized with this disease, individuals with PD also experience a progressive loss in cognitive function (Sawle, 2004). McKeith and colleagues (2004) suggested that as individuals with PD age, risk of developing Parkinson’s Disease Dementia increases and continues to increase as the disease develops. It is important to assess the cognitive function of people with PD as well as the
physical symptoms so that suggested forms of therapy or rehabilitative exercise can address the impairments of the whole person, not just the physical symptoms.

Several studies have examined the effects of exercise and its effects on changing cognitive function in the healthy, aging population (Colcombe et al., 2004; Jedrzewski, Ewbank, Wang, & Trojanowski, 2010; Singh-Manoux, Hillsdon, Brunner, & Marmot, 2005). Colcombe et al. (2004) found that healthy aging individuals who are more fit had greater functional magnetic resonance imaging (fMRI) activity over individuals in a lower fit category. In the same study, fMRI showed that individuals who participated in 45 minutes of group exercise for six months also had greater cerebral blood flow (CBF) and brain activity over individuals living normal daily lives. A 10-year longitudinal study tracked the physical activity and cognitive function in over 1,200 individuals. Results from this study indicated an inverse relationship between exercise and cognitive function decline. This provided evidence that suggested the more active an individual is, the less at risk they are for a decline in cognitive function leading to dementia (Jedrzewski et al., 2010). A second longitudinal study examined physical activity in over 10,000 middle-aged individuals over 11 years and at the end of the 11 years also evaluated cognitive function (Singh-Manoux et al., 2005). The results from this longitudinal study indicated that low levels of physical activity could have been seen as a risk factor for cognitive impairment beginning in middle-aged adults. In addition, this study provided evidence of the neuroprotective effect of exercise on cognitive function.

There have been proposed reasons as to the improvement in cognitive function from exercise. These mechanisms have been inferred in the human population from rat studies. Repeated CVE has been documented to increase capillary density, blood
volume, cardiac contractility, and dopamine production in rats (Lojovich, 2010). These adaptations are difficult to measure in human subjects due to the process of tracking such changes in the human brain. The proposed mechanistic changes can lead to the body’s ability to extract greater amounts of oxygen from the improved blood flow in the brain which can be associated with increased cognitive function.

The effects of exercise in individuals with PD have also been well established in previous studies. Some have focused on balance and fall risk (Allen et al., 2010; Ashburn et al., 2007). Other studies have investigated gait and functional movement outcomes after exercise interventions (Burini et al., 2006; Dibble, Hale, Marcus, Gerber, & LaStayo, 2009; Nieuwboer et al., 2007; Schenkman, Hall, Kumar, & Kohrt, 2008). To date, only two studies have examined the effects on CVE on cognitive function in individuals with PD (Baatile et al., 2000; Cruise et al., 2011; Tanaka et al., 2009). Both Cruise et al. (2011) and Tanaka et al. (2009) used a multi-component exercise program, such as combining strength training and CVE, and found significant improvement in cognitive functions among people with PD. However, neither of these studies specifically investigated the effects of cardiovascular exercise on cognitive functions in individuals with PD.

The purpose of this study is to examine the effects of CVE on cognitive function in individuals with PD. This study can provide scientific evidence that could help clinicians and individuals with PD understand the relationship between CVE and cognitive function. It is valuable to provide evidence-based intervention that is not only focused on the physical symptoms of PD, but on cognitive function in the individual.
LITERATURE REVIEW

*PD*

*Definition and Incidence*

The Mayo Clinic (MC, 2012) defines PD as a progressive nervous system disorder that affects overall movement. PD is also identified by a decrease in dopamine production below normal levels due to the necrosis of dopamine producing cells. Physical symptoms of PD include: bradykinesia (slowness in movement), rigidity (stiffness in muscles), tremors at rest (shaking in muscles), impaired gait (impaired balance and coordination), and diminished expression (quiet voice, softer facial expressions) (Baatile et al., 2000). PD is an idiopathic disease that is seen more prevalently in men, occurs later in life, and has a higher rate of development in those with close relatives who have been diagnosed with PD. While the cause of the necrosis of dopamine producing cells in the substantia nigra of the brain is unknown, links to certain toxins have also been identified as possible contributors to developing PD (MC, 2012). It is estimated that more than one million individuals in the United States are affected by PD (Carne et al., 2005) and that approximately 50,000 – 60,000 new cases of PD are recorded every year (National Parkinson’s disease Foundation [NDF], 2012). According to the Center for Disease Control (CDC, 2012) complications related to PD is the 14th leading cause of death in the United States.

*Pathology*

PD severity is measured using the H&Y scale, which is a five stage scale which examines the degree of impairment from the physical manifestations of the disease. The
H&Y scale ranges from the least severe level of one to the most severe level of five. Stage one is identified by physical symptoms such as tremors on one side of the body (unilateral symptomology), while stage two is determined by physical symptoms on both sides of the body (bilateral symptomology) with no balance impairment. The presence of balance impairment differentiates stage two and three while stages three and four differ in the ability to perform activities of daily living (ADL). Even though ADL are affected in stage four, the individual is still mobile with a walking device. However, at stage five the individual is no longer able to perform ADL and remains in bed or in a wheelchair for transport (Goetz et al., 2004). Traditional care for individuals with PD include pharmacological treatments such as a dopamine supplement, as well as, a surgical procedure known as DBS (McKeith, 2004). These medications and procedure are used to treat the physical manifestations of this disease. As the disease progresses so does the severity of the symptoms which requires either an increase in medication dosage or a medication change (McKeith, 2004). Increasing doses of dopamine are associated with side effects such as involuntary movements or dyskinesia so there are limits to the amount of dopamine that can be used (Sawle, 2004). While PD is characterized by the visible physical manifestations, a progressive decline in cognitive function has also been documented in more recent years (McKeith, 2004).

**PD and Cognitive Function**

PD was initially thought to be a disability in which only physical aspects of the body were affected. However, it is now understood that individuals with PD can also experience a decline in cognitive function throughout the duration of the disease (McKeith, 2004). Along with the deterioration of the dopamine producing cells within
the brain, individuals with PD can also develop Lewy bodies are associated with a loss of cognitive function (Sawle, 2004).

In a study done by Aarsland, Anderson, Larsen, & Lolk (2003) 224 individuals with PD were followed for 8 years during which cognitive function was repeatedly measured. At baseline, approximately 25% of the participants were diagnosed with dementia. By the end of the 8-year study, over 75% of the participants were diagnosed with dementia (Aarsland, Andersen, Larsen, & Lolk, 2003). In this same study, the results from the tests completed at the 4-year data point indicated that individuals with PD were three times as likely to show signs of dementia over healthy individuals.

While most of the current treatments for the manifestations of PD are pharmacological, many of these drugs have side effects that create new challenges for individuals with PD to overcome. Also, due to the progressive nature of the disease, dosages of medications need to be continually increased and changed to meet the increase of the symptoms and side effects (McKeith, 2004; Sawle, 2004). Because PD affects cognitive function, and is a progressive disease, it is important to identify some form of treatment or rehabilitation that could potentially have an effect on the cognitive degeneration of PD.

Exercise and Cognitive Function

While there have been only two published studies on the effects of exercise on cognitive function in PD, there have been several studies examining the effects of exercise on cognitive function in other populations. When examining the effects of exercise and cognitive function, studies tend to focus on older individuals who are
considered healthy with no physiological or psychological impairments. Colcombe et al. (2004) implemented both a cross sectional and a randomized control trial that examined cognitive function between two groups, a high physically fit versus a low physically fit group of individuals. In the same study, cognitive function was measured over a 6-month period between individuals going through aerobic training and those who led lives with low activity. This cross sectional study looked at 41 older individuals of high physical function and assessed their fitness levels through the Rockport one-mile walk test with time used to calculate each individual’s estimated maximum oxygen consumption (VO$_{2\text{max}}$). During a second session, all 41 participants performed cognitive tasks while a fMRI was used to monitor brain activity and CBF. The results of this investigation showed that individuals with a higher calculated VO$_{2\text{max}}$ showed higher brain activity during the cognitive tests. For the randomized control study, 29 participants ($65.50 \pm 5.66$ yrs.) were randomly assigned to either the experimental aerobic exercise group or the control stretching and toning group. Participants in each group exercised three times per week for a maximum of 45 minutes per session for a total of 6 months. Cognitive function was measured 1-week prior and 1 week following the 6-month intervention. The results of this study showed an increase in brain function via fMRI for the participants who were involved in aerobic training.

Information was taken from the National Long Term Care Survey and at the end of 10 years, a total of 1,260 individuals were evaluated. Individuals who participated were considered to be in the elderly population. Both cognitive function assessed by the Mini-Mental State Examination and physical activity levels were recorded at 5-year intervals. At the end of 10 years linear regression analysis showed that the number as well as duration of exercise sessions were inversely associated with cognitive impairment (p=0.002 and p=0.007 respectively).

Another longitudinal study was published in 2005 examining physical activity and cognitive function over a period of 11 years beginning with individuals between 35-55 years old and ending with those individuals between 46-68 years old (Singh-Manoux et al., 2005). In this study a total of 10,308 individuals were examined at five phases throughout the 11-year period. Physical activity was assessed at the first, third, and fifth phases while cognitive function was assessed at baseline and at the fifth phase. Intensity and frequency of physical activity were assessed and five different cognitive tests were used to measure cognitive function. The results of this study indicated that low levels of physical activity have been seen as a risk factor for cognitive impairment beginning in middle-aged adults. While the results seem similar to those from Jedrziewski et al. (2009), Singh-Manoux et al. (2005) began with individuals in a much younger age group and used several different cognitive function tests. Due to the size of this study, the variety of tests used, and the 11-year duration, the results from Singh-Manaux et al. (2005) appear to be more generalizable to a broader age over Jedrziewski et al. (2009), which focused on an older population.
Each of these studies (Colcombe et al., 2004; Jedrziewski et al., 2010; Singh-Manoux et al., 2005) examined the affect that physical activity had on cognitive function in healthy subjects and each of these articles came to the same conclusion: regular physical activity is beneficial to cognitive function.

**Exercise and PD**

Research on the effects of exercise in individuals with PD is limited to effects on the physical manifestations of the disease. There is ample research on how physical activity can reduce fall risk, improve gait, and improve QoL (Allen et al., 2010; Schenkman et al., 2008; van Nimwegen et al., 2011; Yousefi, Tadibi, Khoei, & Montazeri, 2009). Even though each of these studies offers insight in how to combat the physical ramifications of the disease, none of them have a cognitive function component to them.

In a study that examined physical activity levels in individuals with PD, Van Nimwegen et al. (2011) included 699 individuals with PD (of which 76 were randomly chosen for analysis) compared to healthy controls (n=1,959). Those in the PD group were 68.6 (± 7.7) years old with 81.6% classified within H&Y stages of severity two to three, while average disease duration was 5.3 years. The average age of the control group was 65.8 ± 7.0. Individuals in both groups completed a physical activity questionnaire assessing frequency and duration of the activities performed in the two weeks prior to answering the questionnaire. Intensity was determined through assigning each activity a metabolic equivalent for comparison. Linear regression analysis showed that individuals with PD were almost 30% less active then their healthy counterparts. This lack of
physical activity can lead to secondary conditions furthering a decline in physical activity thus negatively affecting QoL and reducing the ability to perform ADL.

Even though Van Nimwegen et al. (2011) demonstrated a lower activity level in individuals with PD, other areas of physical decline in individuals with PD have also been examined. The effect of exercise on fall risk has also been examined in individuals with PD (Allen et al., 2010). Allen et al. (2010) conducted a study in which 48 individuals with PD were randomly assigned to an experimental exercise group or a control group. The average age of those who participated was 66 ± 10. Those who were allocated to the experimental exercise group were instructed to exercise three times per week for 40-60 minutes per session. This protocol lasted for 6 months, with monthly group exercise sessions provided. Those who were assigned to the control group continued their normal daily routines. Linear regression analysis showed trend towards a reduced fall risk score and increased muscle strength. Additional improvement was documented in both a decreased sit to stand time and in the Freezing of Gait questionnaire.

While fall risk is prevalent in individuals with PD and can be improved through exercise (Allen et al., 2010), one aspect that contributes to fall risk is economy of movement. Instead of looking at fall risk, Schenkman, Hall, Kumar, and Kohrt (2008) examined the effects of endurance exercise on economy of movement in individuals with PD. This case study included three participants who ranged in age from 52 – 72 years old and were rated between two to two and a half on the H&Y scale. Each individual completed 4 months of supervised endurance training followed by 12 months of unsupervised endurance training. During the supervised sessions, each participant
exercised three times per week for 40-minute sessions with an initial goal of reaching between 60 – 70% of their maximum heart rate. After the initial 4-month supervised sessions, they were encouraged to exercise five to seven times per week on their own with the goal of reaching 85% of the individual’s maximum heart rate. Investigators used rate of oxygen consumption to measure economy of motion as the primary outcome. The results of this case study indicate that each individual improved economy of motion at one of the four treadmill speeds utilized during testing. The results from this study suggest that individuals with PD can improve economy of motion through the use of endurance training.

While research has demonstrated that individuals with PD are more likely to be less active (van Nimwegen et al., 2011), and that exercise is beneficial in improving fall risk and economy of movement (Allen et al., 2010; Schenkman et al., 2008), Yousefi et al. (2009) published a study examining exercise effects on QoL. This study focused on how QoL and performance of ADL could be altered by exercise in individuals with PD (Yousefi et al., 2009). The researchers recruited 24 individuals with PD (59.8 ± 3.0 years and H&Y stage three) to participate in a 10-week exercise program. Half of the participants were randomly allocated to the exercise group that participated in one-hour, four times per week sessions that included warm-up, flexibility, and strength training for 10 weeks. The other half continued normal daily routines and were offered group education sessions held four times per week during the 10 weeks. The Short Parkinson’s Evaluation scale was used to measure ADL while QoL was measured using the Parkinson’s Disease Quality of Life questionnaire. At the end of the 10 weeks, a Mann-
Whitney U statistical analysis was used and the results indicated that exercise did improve the ability to perform ADL and also improved self-perceived QoL.

While each of the previous studies differed in dependent variables (level of activity, fall risk, economy of motion, and QoL), each study involved some form of exercise as the independent variable. Not only did the studies all involve a similar form of independent variable, but the dependent variables all revolved around some form of physical or emotional aspect of PD.

*Exercise and Cognitive Function in PD*

To date only two articles have been published examining the effects of exercise on cognitive function in PD as the main outcome (Cruise et al., 2011; Tanaka et al., 2009). One study completed by Tanaka et al. (2009) included 20 individuals with PD who were assigned to either the exercise group or the control group. The average participant was 65.4 (± 7.23) years of age and all fell between stage one to three of the H&Y scale. Individuals in the exercise group participated in 6 months of multi-modal exercise (including flexibility, strength, and cardiovascular) 3 times per week for approximately one hour per session. The control group maintained normal daily activities throughout the 6-month protocol. Cognitive function was assessed using the Wisconsin Card Sorting Test while measures of intelligence, anxiety and depression were measured using the Wechsler Adult Intelligence Test, State-Trait Anxiety Inventory, and the Hospital Anxiety and Depression Scale respectively. Only one of these tests is a measurement of cognitive function and it only measures the EF domain of cognitive function. Statistical analysis showed a significant improvement in EF for the exercise
group from pre- to post-intervention but not in the control group. This indicates that multimodal exercise can improve EF in individuals with PD.

Cruise et al. (2011) conducted a similar study to Tanaka et al. (2009) however; Cruise et al. (2011) had 28 participants in which the half allocated to the exercise group (59.47±11.54) participated in resistance and aerobic exercise two times per week for 12 weeks. The control group (60.6±7.34) maintained normal daily routines during the 12-week intervention protocol. The exercise group participated in 60-minute sessions including a warm-up period, strength exercises (increasing in percent repetition maximum (RM) throughout the 12 weeks), and CVE lasting approximately 25 minutes at 60 – 85% maximum heart rate. The H&Y stage between one and three was the same as that in the study done by Tanaka et al. (2009). Cognitive function was measured using the Australian National Adult Reading Test and the Cambridge Neuropsychological Test Automated Battery. Depression was measured via the Geriatric Depression Scale, while QoL was measured with the PDQ39. After conducting paired-t tests, cognitive function showed statistically insignificant improvements and there was no change seen in QoL score. Despite the lack of statistical significance for this study, a trend of cognitive function improvement was indicated in the exercise group even though the measurement tools used were not specifically designed for individuals with PD and shorter intervention duration was implemented over that of Tanaka et al. (2009). Both studies that have examined the effects of exercise on cognitive function in individuals with PD have used a multi-modal exercise approach. Additionally, when measuring cognitive function, neither study used tests designed for individuals with PD.

Summary
PD is an idiopathic disease linked to a reduction in dopamine producing cells within the brain (MC, 2012). Reduction in dopamine production leads to the physical characteristics of the disease such as: tremors at rest, bradykinesia, rigidity, and impaired gait (Baatile et al., 2000). These physical characteristics determine the level of severity the individual is at on the H&Y scale (Goetz et al., 2004). Until recently, researchers did not acknowledge that cognitive function was impaired in individuals with PD (Aarsland et al., 2003; McKeith, 2004; Sawle, 2004).

Research demonstrated that cognitive function can be improved through exercise in the healthy aging population (Colcombe et al., 2004; Jedrziewski et al., 2010; Singh-Manoux et al., 2005). Exercise has also been shown to be beneficial in improving some of the physical characteristics of PD such as economy of motion, fall risk, and QoL (Allen et al., 2010; Schenkman et al., 2008; Yousefi et al., 2009). Despite evidence of exercise benefits on cognitive function in the aging population as well as the exercise benefits on the physical aspects of individuals with PD, only two studies have been published to date that examined the effects on cognitive function from exercise in individuals with PD (Cruise et al., 2011; Tanaka et al., 2009). While both of these studies presented results suggesting the improvement of cognitive function in individuals with PD after an exercise program, neither used strictly aerobic exercise. In addition, the cognitive testing was not designed specifically for individuals with PD or were multiple cognitive tests used to measure different aspects of cognitive function.

Theoretically, isolated aerobic exercise will increase cerebral capillary density, increase cerebral blood flow (CBF) which can increase oxygen supply to the brain, as well as increase dopamine production (Lojovich, 2010). Due to these adaptations and the
findings seen in other publications, it is hypothesized that individuals with PD will improve cognitive function after a 12-week aerobic exercise protocol.
METHODS

Participants

A total of seven male individuals (63.86 yrs ± 4.22) diagnosed with PD were recruited for this study from a university-based adapted exercise center as well as support groups, and clinics. All participants obtained medical clearance prior to participation in this project and were asked to sign an informed consent form. All participants had to meet the following inclusion criteria: a) diagnosis of PD, b) H&Y level between one and three, c) age 40 – 70, d) ability to follow verbal instruction, and e) stable medication protocol for two weeks prior to beginning the study. Participants were excluded from the project if they had the following exclusion criteria a) additional musculoskeletal, neurological, or cardiovascular conditions, and/or b) were currently participating in a structured exercise program on a regular basis.

Research Setting and Design

After recruitment and initial screening were finished, participants were scheduled for pre-intervention data collection. At the beginning of the pre-intervention data collection, participants handed in their medical release and informed consent forms. Once pre-intervention data collection was completed, individuals were assigned to either the CEG or the HSG. After group allocation, individuals began the assigned protocol. All data collection and intervention procedures were the same at each of the four data collection points: a) pre-intervention, b) mid-intervention (4 weeks), c) mid-intervention (8 weeks) and d) post intervention (12 weeks). Each data collection session took place in the same location for each individual.
Research Variables and Instrumentation

Each participant completed two cognitive function tests and a QoL questionnaire at each data collection session. The order remained consistent throughout each session and began with the CNSVS computer neurocognitive test battery. Individuals sat in front of a laptop (the same laptop for each session) and followed the instructions given by the program. This test took approximately 30 minutes to complete and was used to create a detailed assessment of cognitive function.

The second measurement tool was the PDQ-39. This questionnaire is a PD-specific QoL questionnaire composed of 39 questions with answers correlating to frequency of occurrence (i.e. never, occasionally, sometimes, often, and always). The PDQ-39 was used for assessing any changes in participant’s quality of life over eight domains and took approximately 10 minutes to complete. Individuals were instructed to take a break if at any point they felt nervous, pressured, and/or needed to ask a question.

Each data collection session ended with the SCOPA-cog which is a paper-based cognitive function assessment tool specifically designed for individuals with PD. The SCOPA-cog was conducted by the primary researcher. This is a 10-part test and lasted approximately 10 minutes.

In addition to the testing measurement tools, individuals in the CEG used a recumbent bike as the method of CVE. Blood pressure and HR were monitored digitally and recorded every 5 minutes.

Intervention Protocol
The CEG participated in 40 minutes of CVE three times per week for a total duration of 12 weeks. The CVE consisted of a five-minute warm up followed by a 30-minute CV workout at 60 – 75% of the individual’s age-predicted max HR, and ended with a five-minute cool down period. During CVE, the HR, BP, and rate of perceived exertion (RPE) were monitored and recorded every 5 minutes. Participants were asked to schedule exercise session times during the ‘on’ state of medication usage if they were taking a dopamine supplement. This means that individuals needed to exercise and participate in data collection while dopamine supplements were working. Dopamine supplements can wear off prior to the next dose creating a period during which physical characteristics worsen making it difficult to function at an optimal level; this is known as the ‘off’ state.

Individuals in the HSG were given instructions for self-stretching with an illustrated manual and initial demonstration. The participants were asked to perform the stretches three times per week for 12 weeks. Biweekly phone calls were made to monitor adherence and assist individuals with answering possible questions or concerns.

Data Collection Procedures

Participants completed data collection four times throughout the 12-week intervention. In each meeting, the participants were asked to complete the two cognitive function tests measuring specific cognitive function as well as change in cognitive function and the one QoL questionnaire. All tests were administered during the ‘on’ state of their medication schedule if the participant was taking a dopamine supplement. At the first data collection session participants were asked to submit the medical release and
signed informed consent forms. A brief description of each test and overall procedure was provided. Tests were performed in a systematic order for each participant in every data collection session. It began with the CNSVS computer neurocognitive test battery. Once the CNSVS was completed participants were handed the PDQ-39 to fill out. The last of these tests was the SCOPA-cog paper-based cognitive test. Up to a five-minute break between each test was offered to participants and upon completion of all 3 tests participants were free to go.

Statistical Analysis

Data collected from the SCOPA-cog, CNSVS and the PDQ-39 were extracted into Microsoft Excel for further visual analysis.

Human Subjects Protocol

This study protocol was submitted and approved by the University Human Subjects Review Board. All participants were made aware of any potential risks involved in participation when reviewing the informed consent form.
RESULTS

Participant #1

Participant #1 was a 67-year-old male in stage two and a half on the H&Y scale of severity and was assigned to the CEG. Results from CNSVS showed that Participant #1 had improvement in verbal memory, EF, psychomotor speed, and overall cognitive function with a decline seen in reaction time and visual memory. The SCOPA-cog results for Participant #1 revealed an improvement in verbal recall and overall cognitive function and results from the PDQ-39 showed an improvement in overall QoL with no change seen in perceived cognitive impairment. A summary of percent change at each data collection point for each test is listed in Table 1.

Participant #1 had an initial baseline standard score of 100 with a post-intervention score of 118 for an overall 15% improvement in verbal memory with scores at the 4-week and 8-week testing points of 115, and 90 respectively (Figure 1a). Executive function also increased by a total of 15% from pre- to post-intervention with a baseline score of 100 and a post-intervention score of 118 where the score at 4 weeks was 106 and at 8 weeks was 112 (Figure 1b). Psychomotor speed showed steady improvement with a baseline score of 90 and a post-intervention score of 103 for a 10.8% improvement overall and scored a 94 and 96 respectively at 4 and 8 weeks (Figure 1c). Baseline cognitive flexibility score for Participant #1 was 99 with a post- intervention score of 116 for a 14.61% overall improvement with a score of 106 at 4 weeks and 112 at 8 weeks (Figure 1d). Overall cognitive function baseline score for Participant #1 was 97 with a score of 105 post-intervention and intermediate scores of 103 and 102 at the 4- and 8-week testing points for an overall improvement of 6.7% (Figure 1e). Participant #1 did
decline in reaction time with an initial score of 102 and a post-intervention score of 97 for a 4.2% decline (Figure 1f). Visual memory also declined for Participant #1 with a score of 101 at baseline and a score of 90 post-intervention for a 9.2% decline (Figure 1g).

Results from the verbal recall test of the SCOPA-cog reported an initial score of one with a post-intervention score of three for a 40% improvement with scores of two and three at the 4- and 8-week testing points respectively (Figure 1h). Overall cognitive function score at baseline was 20 and the post-intervention score was 23 for an 8.1% improvement with a score of 19 at 4 weeks and 21 at 8 weeks (Figure 1i). Most of the other tests in this measurement tool showed no change from pre- to post-intervention.

In the PDQ-39 Participant #1 had no change in cognitive impairment from pre- to post-intervention (Figure 1j). However, overall QoL score improved from a score of 20.21 to 9.58 for a total 10.63% with a score of 30.52 and 23.91 at the 4- and 8-week testing points respectively.
Figure 1a – Participant #1 verbal memory standardized score at each data collection point

Figure 1b – Participant #1 executive function standardized score at each data collection point
Figure 1c – Participant #1 psychomotor speed standardized score at each data collection point

Figure 1d – Participant #1 cognitive flexibility standardized score at each data collection point
Figure 1e – Participant #1 overall cognitive function standardized score at each data collection point

Figure 1f – Participant #1 reaction time standardized score at each data collection point
Figure 1g – Participant #1 visual memory standardized score at each data collection point

Figure 1h – Participant #1 verbal recall calculated score at each data collection point
Figure 1i – Participant #1 total calculated score at each data collection point

Figure 1j – Participant #1 cognitive impairment domain score at each data collection point
Figure 1k – Participant #1 overall QoL score at each data collection point

Table 1 – Percent change for Participant #1 at each data point where a negative (-) score indicates decline and a (+) score indicates improvement
Participant #2

Participant #2 was a 59-year-old male in stage three of the H&Y scale of severity and was assigned to the CEG. Participant #2 improved in EF, psychomotor speed, reaction time, cognitive flexibility, and overall cognitive function from CNSVS with declines noted in verbal memory and continuous performance. Results from the SCOPA-cog showed improvements in semantic fluency, delayed recall, and overall cognitive function with a decrease in the dice and digit span backwards tests. The PDQ-39 revealed an improvement in overall QoL with no change in perceived cognitive impairment. Percent changes at each testing point for Participant #2 are presented in Table 2.

Participant #2 had an initial CNSVS EF score of 98 with a post-intervention score of 116 for a 15% increase with scores of 51 and 99 at the 4- and 8-week testing points respectively (Figure 2a). Baseline psychomotor speed for Participant #2 was 44 with a post-intervention score of 50 for a 5% overall improvement with midpoint scores of 63 and 61 at 4 and 8 weeks (Figure 2b). Participant #2 had an 18.33% reaction time improvement with a score at baseline of 83 and a post-intervention score of 105 with a 4-week testing point score of 93 and a score of 109 at 8 weeks (Figure 2c). Cognitive flexibility score for Participant #2 improved from a baseline score of 99 to a post-intervention score of 114 with a score of 51 at the 4-week testing point and 93 at the 8-week testing point for an overall 2.5% improvement (Figure 2d). Participant #2 improved by 5% in cognitive function with a baseline score of 87 and a post-intervention score of 93 and scores of 68 and 83 at the 4- and 8-week testing points respectively (Figure 2e). Scores from verbal memory for Participant #2 showed a decline of 5.8%
with scores of 106 and 99 and baseline and post-intervention respectively (Figure 2f). A decline in continuous performance test was also noted for Participant #2 with an initial score of 76 and a post-intervention score of 73 for a 2.5% decline (Figure 2g).

Semantic fluency scores for Participant #2 on the SCOPA-cog improved by a total of 33.33% with a baseline score of four and a post-intervention score of six. Participant #2 had a score of five and six respectively at the 4-week and 8-week testing points (Figure 2h). In delayed recall, Participant #2 had a baseline score of zero with a post-intervention score of two for a 20% improvement with a score of zero at both the 4- and 8-week data collection points (Figure 2i). Participant #2 had a 5.4% increase of overall cognitive function with a baseline score of 25 and a post-intervention score of 27 and scores of 26 and 27 at the 4- and 8-week testing points (Figure 2j). Scores from the dice test did show a decline from the baseline score of three to the post-intervention score of two for 33.33% decline (Figure 2k). Scores from the digit span backward test also declined from four to three baseline to post-intervention for a total decline of 20% (Figure 2l).

Participant #2 showed no change in perceived cognitive impairment (Figure 2m) on the PDQ-39 at any of the 4 testing points however, there was a 2.5% improvement in overall QoL score (Figure 2n). Participant #2 scored a 16.25 at baseline on overall QoL and 13.75 post-intervention with a 4-week score of 15.05 and a score of 12.71 at 8 the 8-week testing point.
Figure 2a – Participant #2 executive function standardized score at each data collection point

Figure 2b – Participant #2 psychomotor speed standardized score at each data collection point
Figure 2c – Participant #2 reaction time standardized score at each data collection point

Figure 2d – Participant #2 cognitive flexibility standardized score at each data collection point
Figure 2e – Participant #2 overall cognitive function standardized score at each data collection point

Figure 2f – Participant #2 verbal memory standardized score at each data collection point
Figure 2g – Participant #2 continuous performance test standardized score at each data collection point

Figure 2h – Participant #2 semantic fluency calculated score at each data collection point
Figure 2i – Participant #2 delayed recall calculated score at each data collection point

Figure 2j – Participant #2 overall cognitive function calculated score at each data collection point
Figure 2k – Participant #2 dice calculated score at each data collection point

Figure 2l – Participant #2 digit span backward calculated score at each data collection point
Figure 2m – Participant #2 cognitive impairment domain score at each data collection point

Figure 2n – Participant #2 overall QoL score at each data collection point
<table>
<thead>
<tr>
<th>Test</th>
<th>4-weeks</th>
<th>8-weeks</th>
<th>12-weeks</th>
<th>Pre to Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Function</td>
<td>-39.17</td>
<td>+40.0</td>
<td>+14.17</td>
<td>+15.0</td>
</tr>
<tr>
<td>Psychomotor Speed</td>
<td>+15.83</td>
<td>-1.67</td>
<td>-9.16</td>
<td>+5.0</td>
</tr>
<tr>
<td>Reaction Time</td>
<td>+8.33</td>
<td>+13.33</td>
<td>-3.33</td>
<td>+18.3</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>-40.0</td>
<td>+35.0</td>
<td>+17.5</td>
<td>+12.5</td>
</tr>
<tr>
<td>Neurocognitive Index</td>
<td>-20.0</td>
<td>+12.5</td>
<td>+12.6</td>
<td>+5.0</td>
</tr>
<tr>
<td>Verbal Memory</td>
<td>-10.83</td>
<td>-36.67</td>
<td>+41.67</td>
<td>-5.8</td>
</tr>
<tr>
<td>Continuous Performance Test</td>
<td>-5.0</td>
<td>-16.67</td>
<td>+19.17</td>
<td>-2.5</td>
</tr>
<tr>
<td>Semantic Fluency</td>
<td>+16.67</td>
<td>+16.67</td>
<td>+0.0</td>
<td>+33.33</td>
</tr>
<tr>
<td>Delayed Recall</td>
<td>+0.0</td>
<td>+0.0</td>
<td>+20.0</td>
<td>+20.0</td>
</tr>
<tr>
<td>Total Score</td>
<td>+2.7</td>
<td>+2.7</td>
<td>+0.0</td>
<td>+5.4</td>
</tr>
<tr>
<td>Dice</td>
<td>+0.0</td>
<td>+0.0</td>
<td>-33.33</td>
<td>-33.33</td>
</tr>
<tr>
<td>Digit Span Backward</td>
<td>+0.0</td>
<td>+20.0</td>
<td>-40.0</td>
<td>-20.0</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>+0.0</td>
<td>+0.0</td>
<td>+0.0</td>
<td>+0.0</td>
</tr>
<tr>
<td>Single Index</td>
<td>+1.2</td>
<td>+2.34</td>
<td>-1.04</td>
<td>+2.5</td>
</tr>
</tbody>
</table>

Table 2 – Percent change for Participant #2 at each data point where a negative (-) score indicates decline and a (+) score indicates improvement.
**Participant #3**

Participant #3 was a 69-year-old male assigned to the CEG with a two and a half H&Y scale of severity. Results from CNSVS test revealed that Participant #3 showed improvement in verbal memory score, EF, attention, and cognitive flexibility with a decline in processing speed and overall cognitive function. Verbal recall, dice, and overall cognitive function scores on the SCOPA-cog improved for Participant #3. Results from the PDQ-39 showed a decline in overall QoL score but an improvement in perceived cognitive impairment. A summary of percent change at each data collection point for Participant #3 on each test is given in Table 3.

Participant #3 experienced an overall improvement of 33.33% in CNSVS verbal memory with a baseline score of 69 and a post-intervention score of 109 with scores of 75 and 90 at the 4- and 8-week testing points respectively (Figure 3a). Participant #3 also improved in EF score from 75 to 82 baseline to post-intervention with intermediate scores of 64 at 4 weeks and 62 at 8 weeks for an overall 5.8% improvement (Figure 3b). Participant #3 had an initial complex attention score of 61 with a post-intervention score of 73 for an overall improvement of 10% with a 4-week score of 58 and a score of 50 at 8 weeks (Figure 3c). Cognitive flexibility scores improved from 72 at baseline to 80 post-intervention with a score of 61 at both the 4- and 8-week testing sessions for an overall improvement of 6.67% (Figure 3d). Decline was noted in the processing speed score of Participant #3 with an initial score of 64 and a post-intervention score of 61 for an overall decline of 2.5% (Figure 3e). Overall cognitive function score also declined for Participant #3 with a score at baseline of 61 and a score of 60 post-intervention for a total decline of 0.83% (Figure 3f).
The SCOPA-cog verbal recall score for Participant #3 improved from a score of zero at baseline to three post-intervention for a total improvement of 40% with a score of zero at both the 4- and 8-week testing points (Figure 3g). On the dice test, Participant #3 improved from a score of one at baseline to a score of 3 post-intervention for an overall 66.67% improvement with a score of three at both the 4- and 8-week testing sessions (Figure 3h). Participant #3 improved in overall cognitive function from a baseline score of six to a post-intervention score of 14 for a total improvement of 21.62% with a score of 10 at the 4-week testing point and a score of 9 at the 8-week testing point (Figure 3i).

Participant #3 did show a decline in overall QoL by 6.9% with an initial score of 29.71 and a post-intervention score of 63.31 (Figure 3j). An improvement in perceived cognitive impairment was noted with a score of 37.50 at baseline and a post-intervention score of 25.00 for a total improvement of 12.5% with a score of 43.75 and 37.50 at the 4- and 8-week testing points respectively (Figure 3k).
Figure 3a – Participant #3 verbal memory standardized score at each data collection point

Figure 3b – Participant #3 executive function standardized score at each data collection point
Figure 3c – Participant #3 complex attention standardized score at each data collection point

Figure 3d – Participant #3 cognitive flexibility standardized score at each data collection point
Figure 3e – Participant #3 processing speed standardized score at each data collection point

Figure 3f – Participant #3 overall cognitive function standardized score at each data collection point
Figure 3g – Participant #3 calculated verbal recall score at each data collection point

Figure 3h – Participant #3 calculated dice score at each data collection point
Figure 3i – Participant #3 overall calculated cognitive function score at each data collection point

Figure 3j – Participant #3 total QoL score at each data collection point
Table 3 – Percent change for Participant #3 at each data point where a negative (-) score indicates decline and a (+) score indicates improvement.
Participant #4

Participant #4 was a 69-year-old male assigned to the HSG and was a stage two on the H&Y scale of severity. Results from CNSVS show a decline in reaction time and continuous performance with improvement noted in complex attention and overall cognitive function. Results from the SCOPA-cog revealed a decline in the indicate cubes, months backwards, and semantic fluency with an improvement in overall cognitive function. Overall QoL declined while no change in perceived cognitive impairment was noted from the results of the PDQ-39. The percent change at each data collection point for Participant #4 on all tests is presented in Table 4.

Participant #4 had a baseline reaction time score of 100 with a score of 89 post-intervention for a total decline of 9.17% with intermediate scores of 95 and 93 at the 4- and 8-week testing points respectively (Figure 4a). Participant #4 also declined in continuous performance with a score at baseline of 87 and a post-intervention score of 77 indicating an 8.33% decline with a score of 84 at 4 weeks and 85 at 8 weeks (Figure 4b). Participant #4 improved by 2.5% in complex attention with a score of 115 at baseline and a post-intervention score of 118 scoring a 117 at both the 4- and 8-week testing points (Figure 4c). Overall cognitive function for Participant #4 improved from a baseline score of 95 to a score of 100 post-intervention for an overall 4.17% improvement with a score of 105 at the 4-week testing session and a 104 at the 8-week testing session (Figure 4d).

Participant #4 scored a four at baseline and at post-intervention scored a three on the SCOPA-cog indicating cubes test for an overall decline of 20% with a score of four at 4 weeks and five at 8 weeks (Figure 4e). The scores from the months backwards test show a decline of 50% for Participant #4 with a score of two at baseline and a score of
one post-intervention with a score of zero at both the 4- and 8-week testing points (Figure 4f). Participant #4 declined by 16.67% in semantic fluency score from a six at baseline to a five post-intervention with a score at 4 weeks of four and at the 8-week testing point a score of 5 was noted (Figure 4g). Improvement in delayed recall was noted in Participant #4 with an initial score of zero and a post-intervention score of four with a score of three at the 4-week testing point and a score of four at 8 weeks for an overall improvement of 80% from pre- to post-intervention (Figure 4h). Overall SCOPA-cog cognitive function score for Participant #4 improved by 5.4% with a score at baseline of 26 and a post-intervention score of 28 and intermediate scores of 23 and 32 at the 4-week and 8-week testing points respectively (Figure 4i).

The results from the PDQ-39 indicate a slight overall decline in QoL with a score at baseline of 18.44 and a post-intervention score of 19.79 for a 1.35% decline with a score of 12.66 and 15.63 at the 4- and 8-week testing points respectively (Figure 4j). There was no change to perceived cognitive impairment for Participant #4 from baseline to post-intervention (Figure 4k).
Figure 4a – Participant #4 standardized reaction time score at each data collection point

Figure 4b – Participant #4 continuous performance standardized score at each data collection point
Figure 4c – Participant #4 complex attention standardized score at each data collection point

Figure 4d – Participant #4 overall cognitive function standardized score at each data collection point
Figure 4e – Participant #4 indicate cubes calculated score at each data collection point

Figure 4f – Participant #4 months backwards calculated score at each data collection point
Figure 4g – Participant #4 semantic fluency calculated score at each data collection point

Figure 4h – Participant #4 delayed recall calculated score at each data collection point
Figure 4i – Participant #4 overall cognitive function calculated score at each data collection point

Figure 4j – Participant #4 overall QoL score at each data collection point
Figure 4k – Participant #4 cognitive impairment domain score at each data collection point

<table>
<thead>
<tr>
<th>Participant #4</th>
<th>4-weeks</th>
<th>8-weeks</th>
<th>12-weeks</th>
<th>Pre to Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction Time</td>
<td>-4.17</td>
<td>-1.67</td>
<td>-3.33</td>
<td>-9.17</td>
</tr>
<tr>
<td>Continuous Performance Test</td>
<td>-2.5</td>
<td>+0.83</td>
<td>-6.67</td>
<td>-8.33</td>
</tr>
<tr>
<td>Complex Attention</td>
<td>+1.67</td>
<td>+0.0</td>
<td>+0.83</td>
<td>+2.5</td>
</tr>
<tr>
<td>Neurocognitive Index</td>
<td>+8.33</td>
<td>-0.83</td>
<td>-3.33</td>
<td>+4.17</td>
</tr>
<tr>
<td>Indicate Cubes</td>
<td>+20.0</td>
<td>+0.0</td>
<td>-40.0</td>
<td>-20.0</td>
</tr>
<tr>
<td>Months Backwards</td>
<td>-100.0</td>
<td>+0.0</td>
<td>+50.0</td>
<td>-50.0</td>
</tr>
<tr>
<td>Semantic Fluency</td>
<td>-33.33</td>
<td>+16.67</td>
<td>+0.0</td>
<td>-16.67</td>
</tr>
<tr>
<td>Delayed Recall</td>
<td>+60.0</td>
<td>+20.0</td>
<td>+0.0</td>
<td>+80.0</td>
</tr>
<tr>
<td>Total Score</td>
<td>-8.1</td>
<td>+24.34</td>
<td>-10.81</td>
<td>+5.4</td>
</tr>
<tr>
<td>Single Index</td>
<td>+5.78</td>
<td>-2.97</td>
<td>-4.16</td>
<td>-1.35</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>+6.25</td>
<td>-6.25</td>
<td>+0.0</td>
<td>+0.0</td>
</tr>
</tbody>
</table>

Table 4 – Percent change for Participant #4 at each data point where a negative (-) score indicates decline and a (+) score indicates improvement
Participant #5

Participant #5 was a 62-year-old male assigned to the HSG and was a two and a half on the H&Y scale of severity. Results from CNSVS test battery indicate that Participant #5 declined in EF, complex attention, cognitive flexibility, and overall cognitive function and improved in reaction time. The SCOPA-cog results indicate a decline in attention but an improvement in overall cognitive function. Improvement in overall QoL and perceived cognitive impairment was noted with results from the PDQ-39. A summary of percent change at each data collection point for Participant #5 on all tests is listed in Table 5.

Participant #5 had an EF baseline score of 100 with a score of 87 post-intervention for an 8.33% overall decline with a score of 90 and 89 at the 4- and 8-week testing sessions respectively (Figure 5a). Complex attention score for Participant #5 at baseline was 82 and post-intervention was 71 with intermediate scores of 79 at 4 weeks and 75 at 8 weeks for an overall decline of 9.17% (Figure 5b). Cognitive flexibility score for Participant #5 at baseline was 96 and at the post-intervention was an 86 for an overall decline of 8.33% with a 4- and 8-week test score of 88 (Figure 5c). An improvement in reaction time for Participant #5 was noted with a score at baseline of 102 and a post-intervention score of 109 for a total improvement of 5.83% and a score of 105 and 97 at the 4- and 8-week testing points respectively (Figure 5d). A decline in overall cognitive function was noted for Participant #5 with a score at baseline of 92 and a post-intervention score of 88 for a 3.33% total decline with a score of 89 at the 4-week data collection point and a 90 at the 8-week testing session (Figure 5e).
The SCOPA-cog attention score for Participant #5 declined by 50% from pre- to post-intervention with a score at baseline of one and a post-intervention score of zero with a 4-week test score of two and a score of zero at the 8-week testing point (Figure 5f). The SCOPA-cog overall cognitive function score improved from a baseline score of 22 to a post-intervention score of 27 for a total improvement of 13.51% with a score at 4 weeks of 26 and a score of 28 at the 8-week testing point (Figure 5g).

The results from the PDQ-39 for Participant #5 indicate an overall improvement in QoL with a score at baseline of 8.18 and a score of 6.83 post-intervention for a 1.35% improvement with intermediate scores of 9.38 and 18.39 at the 4- and 8-week testing points respectively (Figure 5h). Results for perceived cognitive impairment improved overall with an initial score of 12.50 and a score of 6.25 post intervention for an overall 6.25% improvement with a score of 12.5 at the 4-week testing session and a score of 25 at the 8-week testing session.
Figure 5a – Participant #5 standardized executive function score at each data collection point

Figure 5b - Participant #5 standardized complex attention score at each data collection point
Figure 5c – Participant #5 standardized cognitive flexibility score at each data collection point

Figure 5d – Participant #5 standardized reaction time score at each data collection point
Figure 5e – Participant #5 overall cognitive function standardized score at each data collection point

Figure 5f – Participant #5 calculated attention score at each data collection point
Figure 5g – Participant #5 overall cognitive function calculated score at each data collection point

Figure 5h – Participant #5 overall QoL score at each data collection point
Table 5 – Percent change for Participant #5 at each data point where a negative (-) score indicates decline and a (+) score indicates improvement.
Participant #6

Participant #6 was a 63-year-old male assigned to the HSG and was a stage two on the H&Y scale of severity. The results from CNSVS indicate Participant #6 declined in complex attention and cognitive flexibility with an improvement in psychomotor speed and overall cognitive function. SCOPA-cog results noted decline in indicating cubes, attention, fist-edge-palm and overall cognitive function with an improvement in the dice score. Participant #6 improved in overall QoL but declined in perceived cognitive impairment based on results from the PDQ-39. The percent change at each data collection point for Participant #6 on all tests is given in Table 6.

Participant #6 declined by 14.17% in complex attention with a baseline score of 44 and a score of 27 post-intervention with a score of 25 at the 4-week testing point and a 63 at the 8-week data collection point (Figure 6a). Cognitive flexibility score declined from a score of 40 at baseline to a post-intervention score of 37 for a total decline of 2.5% with a score of 35 and 57 at the 4- and 8-week testing points respectively (Figure 6b). Participant #6 did show improvement in psychomotor speed from a baseline score of 54 to a score of 65 post-intervention for a total improvement of 9.17% with a score of 59 at the 4-week testing point and 66 at the 8-week testing point (Figure 6c). Overall cognitive function score for Participant #6 improved from 54 at baseline to 56 post-intervention with intermediate scores of 64 at 4 weeks and 70 at 8 weeks for a total improvement of 1.67% (Figure 6d).

Participant #6 declined in the SCOPA-cog indicating cubes test from a score of three at baseline to a post-intervention score of one for a total decline of 20% with a score
of four at the 4-week testing point and a score of two at the 8-week testing point (Figure 6e). Attention score for Participant #6 declined from one at baseline to zero post-intervention for a total decline of 50% with a score of zero at both the 4- and 8-week testing points (Figure 6f). Participant #6 declined in fist-edge-palm score from two at baseline to zero at the post-data collection test with a score of zero at both the 4- and 8-week testing sessions for a total decline of 66.67% (Figure 6g). An improvement was seen in the dice score for Participant #6 with an initial score of one at baseline and a post-intervention score of two for a total improvement of 33.33% with a score of three at 4 weeks and two at 8 weeks (Figure 6h). In SCOPA-cog overall cognitive function, Participant #6 had a score of 15 at baseline with a post-intervention score of 13 for an overall decline of 5.41% with a score of 16 at the 4-week testing point and a score of 12 at the 8-week testing session (Figure 6i).

Results from the PDQ-39 indicate Participant #6 declined by 18.75% in perceived cognitive impairment with a score at baseline of 25.00 and a post-intervention score of 43.75 with intermediate test scores of 37.5 at 4 weeks and 43.75 at 8 weeks (Figure 6j). Participant #6 improved in overall QoL by 1.46% from a score of 33.91 at baseline to a post-intervention score of 32.45 with a score of 38.75 at the 4-week data collection point and 38.13 at the 8-week data collection point (Figure 6k).
Figure 6a – Participant #6 standardized complex attention score at each data collection point

Figure 6b – Participant #6 standardized cognitive flexibility score at each data collection point
Figure 6c – Participant #6 standardized psychomotor speed score at each data collection point

Figure 6d – Participant #6 overall cognitive function standardized score at each data collection point
Figure 6e – Participant #6 calculated indicate cubes score at each data collection point.

Figure 6f – Participant #6 calculated attention score at each data collection point.
Figure 6g – Participant #6 calculated fist-edge-palm score at each data collection point

Figure 6h – Participant #6 calculated dice score at each data collection point
Figure 6i – Participant #6 overall calculated cognitive function at each data collection point

Figure 6j – Participant #6 cognitive impairment domain score at each data collection point
Figure 6k – Participant #6 overall QoL score at each data collection point

<table>
<thead>
<tr>
<th>Participant #6</th>
<th>4-weeks</th>
<th>8-weeks</th>
<th>12-weeks</th>
<th>Pre to Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex Attention</td>
<td>-15.83</td>
<td>+31.67</td>
<td>-30.0</td>
<td>-14.17</td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>-4.17</td>
<td>+18.33</td>
<td>-16.67</td>
<td>-2.51</td>
</tr>
<tr>
<td>Psychomotor Speed</td>
<td>+3.33</td>
<td>+5.83</td>
<td>-0.83</td>
<td>+9.17</td>
</tr>
<tr>
<td>Neurocognitive Index</td>
<td>+8.33</td>
<td>+5.0</td>
<td>-11.67</td>
<td>+1.67</td>
</tr>
<tr>
<td>Indicate Cubes</td>
<td>+20.0</td>
<td>-20.0</td>
<td>-20.0</td>
<td>-20.0</td>
</tr>
<tr>
<td>Attention</td>
<td>-50.0</td>
<td>+0.0</td>
<td>+0.0</td>
<td>-50.0</td>
</tr>
<tr>
<td>Fist-Edge-Palm</td>
<td>-66.67</td>
<td>+0.0</td>
<td>+0.0</td>
<td>-66.67</td>
</tr>
<tr>
<td>Dice</td>
<td>+66.67</td>
<td>-33.33</td>
<td>+0.0</td>
<td>+33.33</td>
</tr>
<tr>
<td>Total Score</td>
<td>+2.7</td>
<td>-10.81</td>
<td>+2.7</td>
<td>-5.41</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>-12.5</td>
<td>-6.25</td>
<td>+0.0</td>
<td>-18.75</td>
</tr>
<tr>
<td>Single Index</td>
<td>-4.84</td>
<td>+0.59</td>
<td>+5.68</td>
<td>+1.46</td>
</tr>
</tbody>
</table>

Table 6 – Percent change for Participant #6 at each data point where a negative (-) score indicates decline and a (+) score indicates improvement
Participant #7

Participant #7 was a 58-year-old male assigned to the HSG and at stage one and a half of the H&Y scale of severity. Results for Participant #7 from CNSVS test battery indicated a decline in reaction time score, continuous performance test, and processing speed, with slight improvement in psychomotor speed and overall cognitive function. Participant #7 declined in the indicating cubes test and the fist-edge-palm test with improvement seen in delayed recall and overall cognitive function according to the results from the SCOPA-cog. Results from the PDQ-39 indicated Participant #7 declined in both overall QoL and perceived cognitive impairment domain score. A summary of the percent change at each of the testing points in all tests for Participant #7 are in Table 7.

Reaction time score decreased by a total of 5% with an initial score of 116 at baseline to a post-intervention score of 110 with a 4-week test score of 102 and a score at 8 weeks of 112 (Figure 7a). Participant #7 declined in continuous performance test score from a baseline score of 100 to a post-intervention score of 96 for an overall decline of 3.33% with a score of 98 and 94 at the 4- and 8-week testing points respectively (Figure 7b). Processing speed declined by 0.83% from a baseline score of 107 to a post-intervention score of 106 with a score of 118 at the 4-week testing point and a score of 94 at the 8-week testing session (Figure 7c). Participant #7 had an overall improvement of 2.5% in psychomotor speed from a baseline score of 93 to a post-intervention score of 96 with a score of 98 and 91 at the 4- and 8-week intermediate testing points respectively (Figure 7d). Overall cognitive function improved for Participant #7 from a baseline score
of 101 to a post-intervention score of 104, a total increase of 2.5%, with a score of 100 at the 4-week testing session and a score of 101 at 8 weeks (Figure 7e).

Results from the SCOPA-cog indicate cubes test show that Participant #7 declined from a baseline score of five to a post-intervention score of four for a total decline in 20% with a score of five at both the 4- and 8-week intermediate testing sessions (Figure 7f). Participant #7 declined by a total of 33.33% in fist-edge-palm test with a baseline score of three and a post-intervention score of two where a score of three was noted at the 4- and 8-week testing sessions (Figure 7g). Participant #7 had an overall improvement of 80% in delayed recall with a baseline score of zero and a post-intervention score of four with an intermediate score of four at both the 4- and 8-week test sessions (Figure 7h). Overall cognitive function score for Participant #7 improved from a baseline score of 27 to a post-intervention score of 31 for a total improvement of 10.81% with a score of 28 at the 4-week data collection point and a score of 34 at the 8-week testing point (Figure 7i).

Overall QoL declined by 12.92% from a score of 20.73 at baseline to a post-intervention score of 33.65 with a score of 24.58 and 27.34 at the 4- and 8-week testing points respectively (Figure 7j). Perceived cognitive impairment score declined from a score of 12.50 at baseline to a post-intervention score of 18.75 for a total decline of 6.25% with a score of 18.75 at both the 4- and 8-week intermediate testing sessions (Figure 7k).
Figure 7a – Participant #7 standardized reaction time score at each data collection point

Figure 7b – Participant #7 standardized continuous performance test at each data collection point
Figure 7c – Participant #7 standardized processing speed score at each data collection point.

Figure 7d – Participant #7 standardized psychomotor speed score at each data collection point.
Participant #7

Figure 7e – Participant #7 overall cognitive function standardized score at each data collection point

Participant #7

Figure 7f – Participant #7 calculated indicate cubes score at each data collection point
Figure 7g – Participant #7 fist-edge-palm calculated score at each data collection point

Figure 7h – Participant #7 calculated delayed recall score at each data collection point
Figure 7i – Participant #7 overall calculated cognitive function score at each data collection point

Figure 7j – Participant #7 overall QoL score at each data collection point
Table 7 – Percent change for Participant #7 at each data point where a negative (-) score indicates decline and a (+) score indicates improvement.
Group Results

Group results were determined by averaging the scores of the individuals assigned to each group at each data collection point for each measurement. By visual analysis, the CEG showed greater improvement in EF, complex attention, and cognitive flexibility. Results from overall cognitive function indicate that both the CEG and HSG improved in overall cognitive function. Results from the SCOPA-cog indicate that the CEG had a greater improvement over the HSG in verbal recall as well as overall cognitive function and the CEG improved while the HSG declined in the indicating cubes and months backwards tests. Improvement in both overall QoL and perceived cognitive impairment was noted in the PDQ-39 for the CEG while those in the HSG declined in both aspects. A summary of the percent change at each data collection point for the groups is outlined in Table 8.

EF scores improved by 11.94% for the CEG from a baseline score of 91.00 to 105.33 with intermediate scores of 73.67 and 91.00 at the 4- and 8-week testing points respectively while the HSG improved by 4.5% with an initial score of 90.75 at baseline to a post-intervention score of 95.25 with a 4-week score of 93.00 and an 8-week score of 94.50 (Figure 8a). Complex attention scores for the CEG showed an overall improvement 6.39% from a score of 88.33 at baseline to a post-intervention score of 96.00 with a score of 70.33 at 4 weeks and a score of 74.33 at 8 weeks while the HSG declined from a baseline score of 84.25 to a post-intervention score of 79.50 for an overall decline of 3.96% with a score of 80.00 and 87.75 at the 4- and 8-week testing points respectively (Figure 8b). The CEG improved by 11.1% in cognitive flexibility with an initial score of 90 and a post-intervention score of 103.33 with intermediate
scores of 72.67 at 4 weeks and 88.67 at 8 weeks while the HSG improved by 1.45% with a score at baseline of 88.75 and a post-intervention score of 90.50 with a score of 87.25 at the 4-week testing point and 93.50 at the 8-week testing point (Figure 8c). Overall cognitive function improved by 3.61% in the CEG with a score at baseline of 81.67 and a post-intervention score of 86.00 with a score at the 4-week testing point of 75.33 and an 8-week testing score of 80.67 while the HSG improved by 1.25% from an initial score of 85.50 and a post-intervention score of 87.00 with a score of 89.50 and 91.25 at the 4-week and 8-week testing points respectively (Figure 8d).

Verbal recall scores improved by 33.4% in the CEG from an initial baseline score of 1.33 to a post-intervention score of 3.00 with a 4-week testing score of one and an 8-week testing score of 1.67 while the HSG improved by 20% scoring a 2.50 at baseline and scoring a 3.50 post-intervention with intermediate scores of 2.25 and three at the 4- and 8-week testing points respectively (Figure 8e). Analysis of the results from the indicate cubes test showed an overall improvement of 6.6% for the CEG with an initial score of three and a post-intervention score of 3.33 with a score of three at both the 4- and 8-week testing points while the HSG declined by 20% with a baseline score of 4.25 and a post-intervention score of 3.25 with a score of 4.25 at the 4-week testing session and a score of 3.75 at 8 weeks (Figure 8f). Results from the months backwards test showed an improvement of 17% for the CEG with an initial score of 1.33 at baseline and a score of 1.67 post-intervention with a score of 1.67 at both the 4- and 8-week intermediate testing points where the HSG showed no change from baseline to post-intervention scores (Figure 8g). Overall cognitive function showed an 11.7% improvement for the CEG with a score of 17.00 at baseline and a post-intervention score
of 21.33 with a score of 18.33 at the 4-week testing point and 19.00 at the 8-week testing point while the HSG improved by 6.08% from a baseline score of 22.50 to a score of 24.75 post-intervention with a score of 23.25 and 26.50 at 4 and 8 weeks respectively (Figure 8h).

Perceived cognitive impairment improved by 4.17% for the CEG from as baseline score of 18.75 to a post-intervention score of 14.58 with a score of 25.00 at the 4-week testing point and a score of 22.92 at the 8-week testing point while the HSG declined by 4.69% with a score at baseline of 25.00 and a post-intervention score of 29.69 with a score of 28.13 at 4 weeks and a score of 34.38 at 8 weeks (Figure 8i). Individuals in the CEG improved overall QoL by 2.08% with a score at baseline of 22.06 and a post-intervention score of 19.98 and a score of 28.56 and 20.75 at the 4- and 8-week testing session respectively while the HSG declined from an initial score of 20.31 to a post-intervention score of 23.18 for an overall decline of 2.87% with a score of 21.34 at the 4-week testing session and a score of 24.87 at the post-intervention testing session (Figure 8j).
Figure 8a – Group average standardized scores for executive function at each data collection point

Figure 8b – Group average standardized scores for complex attention at each data collection point
Figure 8c – Group average standardized scores for cognitive flexibility at each data collection point

Figure 8d – Group average standardized scores for overall cognitive function at each data collection point
Figure 8e – Calculated group averages for verbal recall at each data collection point

Figure 8f – Calculated group averages for indicate cubes at each data collection point
Figure 8g – Calculated group averages for months backwards at each data collection point

Figure 8h – Calculated group averages for overall cognitive function at each data collection point
Figure 8i – Group average cognitive impairment domain scores at each data collection point

Figure 8j – Group averages overall QoL at each data collection point
<table>
<thead>
<tr>
<th>Group Results</th>
<th>4-weeks</th>
<th>8-weeks</th>
<th>12-weeks</th>
<th>Pre to Post</th>
<th>CEG-HSG Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Function</td>
<td>CEG -14.44</td>
<td>+14.44</td>
<td>+11.94</td>
<td>+11.94</td>
<td>+7.44</td>
</tr>
<tr>
<td></td>
<td>HSG +1.88</td>
<td>+1.25</td>
<td>+0.63</td>
<td>+4.5</td>
<td></td>
</tr>
<tr>
<td>Complex Attention</td>
<td>CEG -15.0</td>
<td>+3.78</td>
<td>+18.06</td>
<td>+6.93</td>
<td>+10.89</td>
</tr>
<tr>
<td></td>
<td>HSG -3.54</td>
<td>+6.46</td>
<td>+6.88</td>
<td>-3.96</td>
<td></td>
</tr>
<tr>
<td>Cognitive Flexibility</td>
<td>CEG -14.44</td>
<td>+13.33</td>
<td>+12.22</td>
<td>+11.1</td>
<td>+9.65</td>
</tr>
<tr>
<td></td>
<td>HSG -1.25</td>
<td>+5.21</td>
<td>-2.5</td>
<td>+1.45</td>
<td></td>
</tr>
<tr>
<td>Neurocognitive Index</td>
<td>CEG -5.28</td>
<td>+4.45</td>
<td>+4.44</td>
<td>+3.61</td>
<td>+2.36</td>
</tr>
<tr>
<td></td>
<td>HSG +3.33</td>
<td>+1.46</td>
<td>-3.54</td>
<td>+1.25</td>
<td></td>
</tr>
<tr>
<td>Verbal Recall</td>
<td>CEG -6.6</td>
<td>+13.4</td>
<td>+26.6</td>
<td>+33.4</td>
<td>+13.4</td>
</tr>
<tr>
<td></td>
<td>HSG -8.0</td>
<td>+15.0</td>
<td>+10</td>
<td>+20.0</td>
<td></td>
</tr>
<tr>
<td>Indicate Cubes</td>
<td>CEG +0.0</td>
<td>+0.0</td>
<td>+6.6</td>
<td>+6.6</td>
<td>+26.6</td>
</tr>
<tr>
<td></td>
<td>HSG +0.0</td>
<td>-10.0</td>
<td>-10.0</td>
<td>-20.0</td>
<td></td>
</tr>
<tr>
<td>Months Backwards</td>
<td>CEG +17.0</td>
<td>+0.0</td>
<td>+0.0</td>
<td>+17.0</td>
<td>+17.0</td>
</tr>
<tr>
<td></td>
<td>HSG +0.0</td>
<td>-12.5</td>
<td>+12.5</td>
<td>+0.0</td>
<td></td>
</tr>
<tr>
<td>Total Score</td>
<td>CEG +3.59</td>
<td>+2.08</td>
<td>+3.59</td>
<td>+11.7</td>
<td>+5.62</td>
</tr>
<tr>
<td></td>
<td>HSG +2.03</td>
<td>+8.78</td>
<td>-1.46</td>
<td>+6.08</td>
<td></td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>CEG -6.25</td>
<td>+2.08</td>
<td>+8.34</td>
<td>+4.17</td>
<td>+8.86</td>
</tr>
<tr>
<td></td>
<td>HSG -3.13</td>
<td>-6.25</td>
<td>+4.69</td>
<td>-4.69</td>
<td></td>
</tr>
<tr>
<td>Single Index</td>
<td>CEG -6.5</td>
<td>+7.81</td>
<td>+0.77</td>
<td>+2.08</td>
<td>+4.95</td>
</tr>
<tr>
<td></td>
<td>HSG -1.03</td>
<td>-3.53</td>
<td>+1.69</td>
<td>-2.87</td>
<td></td>
</tr>
</tbody>
</table>

Table 8 – Percent change for the CEG and the HSG at each data point where a negative (-) score indicates decline and a (+) score indicates improvement
The results from this study indicate that while both stretching and CVE might improve selective aspects of cognitive function, a greater improvement in cognitive function could be demonstrated through CVE as opposed to stretching alone. Greater numeric improvements to memory, EF, and QoL in the CEG over the HSG were seen. These results are similar to those found by Cruise et al. (2011) for improvement in cognitive function. Similar results to QoL were also documented by Baatile et al. (2000) from the PDQ-39 after moderate exercise indicating that exercise may have a positive effect on QoL in individuals with PD.

CEG

All three participants showed improvement in EF (Figures 1b, 2a, and 3b), cognitive flexibility (Figures 1d, 2d, and 3d) and SCOPA-cog overall cognitive function (Figures 1i, 2j, and 3j). Similar results were seen by Cruise et al. (2011) and Tanaka et al. (2008) with regard to improvements in EF after exercise in PD. Participants #1 and #2 improved overall QoL (Figures 1k and 2n) while perceived cognitive impairment (Figures 1j and 2m) showed no change. Participant #3 had improvement in perceived cognitive impairment (Figure 3l) but overall QoL (Figure 3k) declined. Participants #1 and #2 did have medication changes over the 12-week intervention period while Participant #3 had no medication changes which could be responsible for score changes at the different testing points. Medication changes are made frequently for individuals with PD and while these medications are used to treat the physical characteristics of PD,
the ability to respond efficiently to questions might be impacted by inconsistencies from such medication changes (Katzenschlager & Lees, 2002).

A consistent decline at the 4-week testing point for Participant #2 was seen, however, this could be due to the inability to utilize his right arm during the testing session because it was caught on the armrest of the chair he was sitting in. This was not made known until after completing testing for that session. Participant #3, had declines documented on several tests at the 8-week data collection point. This could likely be due to a desire by the subject at that time to quit the study, however, he was encouraged to complete the study by his significant other. Another observation for Participant #3 is a reduced need to use a cane by the end of the 12-week intervention.

The improvements seen in EF, cognitive flexibility, and overall cognitive function in each of the participants in the CEG could be a result of increased cerebral capillary density (Van der Borght et al., 2009), CBF (Smith et al., 2012), or dopamine production (Sutoo & Akiyama, 2003). One, or a combination of the three, could explain the improvements noted from each participant. The decline documented in the results could be due to the progressive nature of PD (McKeith, 2004; Sawle, 2004), medication inconsistencies, or even elevated stress levels on the day of testing (Henckens, van Wingen, Joëls, & Guillén, 2012).

Participants #1, #2, and #3 showed improvement in overall QoL or in perceived cognitive impairment. These results are in agreement with Baatile et al. (2010) that exercise can improve QoL in individuals with PD (Baatile et al., 2000).
All four participants in the HSG had both improvements and declines on different tests throughout the 12-week intervention. Despite decline in some of the individual cognitive function tests, each participant showed varying levels of improvement in overall cognitive function on either the CNSVS or the SCOPA-cog or both (Figure 4d, 4j, 5g, 6e, 7e, and 7i). Similar to those in the CEG, all individuals in the HSG had medication changes throughout the 12 weeks which could account for some of the score changes seen. The duration of disease could also be a factor in overall cognitive function with a longer duration of disease correlated with worsening cognitive function (Aarsland et al., 2003). One study by Hotting et al. (2012) showed a greater improvement in EF of individuals in a stretching protocol over individuals in an aerobic cycling protocol (Hötting et al., 2012). Colcombe et al (2004) conducted a similar study and found that individuals in the stretching protocol did have improvements in cognitive function along with those in an exercise group.

Overall QoL and perceived cognitive impairment showed similar fluctuations to the cognitive function results between participants in the HSG. Despite seeing improvements in overall cognitive function, both Participant #6 and #7 reported decline in perceived cognitive function (Figure 6k and 7k). This could be because the improvements in cognitive function were too minimal to be detected by the individual participant in order to change perception of cognitive impairment. For Participant #4, perceived cognitive impairment showed no change (Figure 4k) and Participant #5 indicated an improvement in perceived cognitive impairment (Figure 5i). The
improvement seen by Participant #5 could be due to a lack of any regular physical activity prior to starting this protocol to performing stretches on a regular basis.

Groups

Both groups showed improvement in overall cognitive function (Figure 8d) however; the CEG tended to show a greater amount of improvement compared to the HSG. These results are similar to the results found by Colcumbe et al. (2004). In terms of medication changes, participants in both groups experienced some form of medication change whether it was a dosage increase or a different medication altogether. Since both groups had medication changes, a greater improvement in the CEG might not be due to medication but could potential be due to physiological adaptations. These physiological adaptations can include an increase in: cerebral capillary density, CBF, and/ or dopamine production.

The changes found in overall QoL and perceived cognitive impairment (Figure 8j, 8i) could be due to several factors in both the CEG and the HSG. These factors include medication changes, high stress during testing, or the protocol each individual was a part of. For individuals in the HSG, overall QoL and cognitive impairment could have declined due to a perception that stretching would have no merit on cognitive function or from a belief that only traditional pharmaceuticals could affect the symptoms of PD. This measurement could have improved for individuals in the CEG because of a perception that CVE would improve QoL and cognitive impairment.

Adherence
All seven participants had a 100% adherence rate throughout the intervention. Individuals in the CEG were offered make-up sessions at the end of the study to make up any previously missed sessions. In addition, individuals in the HSG verbally accounted for individual sessions via bi-weekly phone calls made by the primary investigator. Due to transportation issues and medication effects, individuals in the CEG had more sessions to make up for over individuals in the HSG.

Limitations

Limitations for this study include a small sample size, medication changes, and the progressive nature of PD. A larger sample size could provide more generalized results. If medications did not have to be changed, any results seen could be more related to the protocol instead of the medications, however, the progressive nature of PD does not make this feasible. The progressive nature of PD provides a challenge on its own since both physical and cognitive function is continually worsening and while improvement might not be seen, any maintenance of function can be considered a notable finding.

Future Research

As this study was a multi-modal case study, further research with a larger population is needed to document potentially generalized results on the implications of CVE on cognitive function for individuals with PD. In addition, future studies should try to provide funding to provide compensation for those who would otherwise not be able to participate in such a study should be considered. Future studies might want to consider a longer intervention period to allow for more pronounced physiological changes to occur.
as well as the use of a fMRI to aid in seeing these potential adaptations. A log should be considered for individuals in a home exercise protocol to keep track of specific exercises done, length of time, personal observations of the individual, and for detailed adherence records.

**Conclusion**

In summary, the results from this study suggest that individuals with PD can have individual improvements in some aspects of cognitive function from CVE or stretching although greater improvements have been seen from CVE. Therefore, CVE should be considered as a large part of a weekly rehabilitation program recommended by clinicians and health care specialists when making exercise recommendations for individuals with PD.
REFERENCES


### APPENDIX A

#### Age Distribution

<table>
<thead>
<tr>
<th>AGE</th>
<th>CEG</th>
<th>HSG</th>
<th>GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>59</td>
<td>63</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>67</td>
<td>69</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>69</td>
<td>62</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>69</td>
<td></td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>62</td>
<td></td>
<td>58</td>
<td></td>
</tr>
</tbody>
</table>

**AVG AGE** | **65** | **63** | **63.86**
**SD** | **4.32** | **3.94** | **4.22**

Table 9: Age distribution of the CEG, HSG, and overall group

#### H&Y Distribution

<table>
<thead>
<tr>
<th>H&amp;Y</th>
<th>CEG</th>
<th>HSG</th>
<th>GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>2</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>2</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>2</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5</td>
<td></td>
</tr>
</tbody>
</table>

**AVG H&Y** | **2.67** | **2.00** | **2.29**
**SD** | **0.24** | **0.35** | **0.45**

Table 10: H&Y Distribution of the CEG, HSG, and overall group
<table>
<thead>
<tr>
<th></th>
<th>Improved</th>
<th>Declined</th>
<th>Maintained</th>
<th>% Improve</th>
<th>% Decline</th>
<th>% Maintain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CNSVS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEG</td>
<td>20</td>
<td>11</td>
<td>2</td>
<td>60.61</td>
<td>33.33</td>
<td>6.06</td>
</tr>
<tr>
<td>HSG</td>
<td>24</td>
<td>16</td>
<td>4</td>
<td>54.55</td>
<td>36.36</td>
<td>9.09</td>
</tr>
<tr>
<td><strong>SCOPA-cog</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEG</td>
<td>12</td>
<td>2</td>
<td>16</td>
<td>40.00</td>
<td>6.67</td>
<td>53.33</td>
</tr>
<tr>
<td>HSG</td>
<td>16</td>
<td>11</td>
<td>13</td>
<td>40.00</td>
<td>27.50</td>
<td>32.50</td>
</tr>
<tr>
<td><strong>PDQ-39</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEG</td>
<td>13</td>
<td>6</td>
<td>8</td>
<td>48.15</td>
<td>22.22</td>
<td>29.63</td>
</tr>
<tr>
<td>HSG</td>
<td>13</td>
<td>19</td>
<td>4</td>
<td>36.11</td>
<td>52.78</td>
<td>11.11</td>
</tr>
</tbody>
</table>

Table 11: Number and percent of improved, declined, and maintained scores on all test questions for each group
APPENDIX B

12 individuals assessed for eligibility

10 individuals randomized into CEG or HSG

6 Allocated to CEG

3 Individuals dropped due to time commitment

3 Analyzed

6 Allocated to HSG

2 Individuals dropped due to being allocated to HSG

4 Analyzed

Figure 9: Flow chart of recruitment through analyzation
APPENDIX C

California State University, Northridge
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

The Effects of Cardiovascular Exercise on Cognitive Function in Individuals with Parkinson's Disease

You are being asked to participate in a research study. Participation in this study is completely voluntary. Please read the information below and ask questions about anything that you do not understand before deciding if you want to participate. A researcher listed below will be available to answer your questions.

RESEARCH TEAM

Researcher:  
Jessica McCamish  
Kinesiology  
818-677-7210  
805-660-1146

Faculty Advisor: Dr. Taeyou Jung
Director, Adapted Therapeutic Exercise Program
Kinesiology
18111 Nordhoff St.
Northridge, CA 91330-8287

PURPOSE OF STUDY
The purpose of this research is to examine the effects of cardiovascular exercise on cognitive function in individuals with Parkinson’s Disease (PD).

SUBJECTS

Inclusion Requirements
You are eligible to participate in this study if you have been diagnosed with Idiopathic Parkinson’s Disease with a Hoehn and Yahr stage between 1-2.5, are between 40-70 years of age, are able to participate in approximately 40-minute cardiovascular exercise, are able to read, communicate, and follow directions in English, and operate a computer mouse.

Exclusion Requirements
You are not eligible to participate in this study if you have additional musculoskeletal or neurological condition or cardiovascular disorder that could hinder your ability from participating in cardiovascular exercise, exceed the Hoehn and Yahr severity number, do
not meet the age requirement, and/or cannot work a mouse or communicate or read in English.

*Time Commitment*

The length of exercise participation will require 15-weeks with three 40-minute sessions per week of your time. It will also require 4 sessions of cognitive function testing by performing such tasks as number or word recognition or matching exercises.

**PROCEDURES**

*Recruitment*

Upon being recruited for this study, you will be required to obtain medical clearance from your primary physician prior to any cognitive function tests (such as memory tests). Once medical clearance has been obtained, you will be randomly assigned to either the cardiovascular group or the home-exercise group.

*Initial Meeting*

After you have obtained medical clearance you will be directed to come to the Center of Achievement through Adapted Physical Activity on the California State University, Northridge campus for a brief one-on-one explanation of the cognitive function tests used as well as an explanation of which group you have been assigned into and what participation in that group entails. After this initial meeting the first data-collection will take place.

*Data collection procedures*

All data collection and cardiovascular sessions will be held at the CoA, CSUN. Data collection procedures will last approximately 1 hour and will include:

a.) You will be asked to complete a questionnaire about your overall quality of life.

b.) You will be asked to perform a short paper-based test that will measure your overall cognitive functions, asking questions about how well you can remember things and how quickly you can answer questions correctly.

c.) You will be asked to complete a computer-based test that will examine your specific cognitive functions such as reaction time and decision making skills.

*Intervention Procedures*

You will perform approximately 40 minutes of cardiovascular exercise using a recumbent stationary bike 3 times a week for 15-weeks. Heart rate (HR), blood pressure (BP), and Rate of Perceived Exertion will be continually monitored by clinical staff.

If you are randomly assigned to the home-based exercise group, you will be provided with a stretching program consistent in duration (approximately 40 minutes) with that of the cardiovascular exercise group. Initially, orientation will be provided with specific instructions on how to perform the stretches provided. Weekly phone calls will be made to monitor adherence and safety.

Data collection will be held at the pre, 5-week, 10-week, and post-intervention intervals. Each data collection session will last approximately 1 hour.
RISKS AND DISCOMFORTS
While you understand that we strive to prevent any possible complications or injuries, there are risks involved in participation such as:
- Cardiovascular complications
- Dehydration
- Falling
- Sprains
- Broken Bones
- Physical fatigue
- Muscle cramps
- Emotional distress
In an attempt to minimalize these risks, certain precautions will be taken such as:
- Physician clearance will be obtained to ensure you do not have any contraindications for the exercise protocol
- You will be asked to drink plenty of water in order to keep themselves hydrated during the intervention
- Research assistants will be used as active spotters during the transition from the Lobby to the equipment and off then back to the lobby at the conclusion of the exercise session.
- You will be encouraged to take a break should they experience physical fatigue.
- Emergency services (911) will be contacted and you will be referred to their primary care physician
- You will be allowed to stop at anytime during the tests or questionnaire should you feel distressed or concerned. You should feel free to ask questions or address concerns during these tests.

BENEFITS
Subject Benefits
The benefits of this project will be having you complete an organized exercise program, preparing you for community-based fitness programs, and teaching you the benefits to your overall health that exercise can provide.

Benefits to Others or Society
The study findings can contribute to building scientific evidence for treating individuals with PD.

ALTERNATIVES TO PARTICIPATION
The only alternative to participation in this study is not to participate.

COMPENSATION, COSTS AND REIMBURSEMENT
Compensation for Participation
You will not be paid for your participation in this research study.
**Costs**
There is no cost to you for participation in this study.

**Reimbursement**
Since there is no cost to you there will be no need for reimbursement.

**WITHDRAWAL OR TERMINATION FROM THE STUDY AND CONSEQUENCES**
You are free to withdraw from this study at any time. **If you decide to withdraw from this study you should notify the research team immediately.** The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, or if your safety and welfare are at risk.

**CONFIDENTIALITY**

*Subject Identifiable Data*
All identifiable information that will be collected about you will be removed and replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data.

*Data Storage*
All electronic research data will be stored on a laptop or desktop computer that is password protected.

All paper research data will be stored in a locked file cabinet at the Center of Achievement through Adapted Physical Activity in the main office where only the primary investigator, Jessica McCamish, and faculty advisor, Dr. Taeyou Jung have access.

Both forms of data will remain accessible to the primary researcher and the faculty advisor up to three years after the completion of the study after which all data will be destroyed.

*Data Access*
The researcher and faculty advisor named on the first page of this form will have access to your study records. Any information derived from this research project that personally identifies you will not be voluntarily released or disclosed without your separate consent, except as specifically required by law. Publications and/or presentations that result from this study will not include identifiable information about you.

*Data Retention*
The researchers intend to keep the research data for approximately 3 years and then it will be destroyed.
IF YOU HAVE QUESTIONS
If you have any comments, concerns, or questions regarding the conduct of this research please contact the research team listed on the first page of this form.

If you are unable to reach a member of the research team listed on the first page of the form and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact Research and Sponsored Projects, 18111 Nordhoff Street, California State University, Northridge, Northridge, CA 91330-8232, or phone 818-677-2901.

VOLUNTARY PARTICIPATION STATEMENT
You should not sign this form unless you have read it and been given a copy of it to keep. Participation in this study is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with California State University, Northridge. Your signature below indicates that you have read the information in this consent form and have had a chance to ask any questions that you have about the study.

I agree to participate in the study.

___________________________________________________  __________________
Subject Signature                  Date

___________________________________________________
Printed Name of Subject

___________________________________________________  __________________
Researcher Signature                Date

___________________________________________________
Printed Name of Researcher
APPENDIX D
CALIFORNIA STATE UNIVERSITY, NORTHRIDGE

EXPERIMENTAL SUBJECTS

BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1) To be told what the study is trying to find out,

2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,

3) To be told about the frequent and/or important risks, side effects or discomforts of the things that will happen to me for research purposes,

4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,

5) To be told the other choices I have and how they may be better or worse than being in the study,

6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,

7) To be told what sort of medical treatment (if needed) is available if any complications arise,

8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study.

9) To receive a copy of the signed and dated consent form.

10) To be free of pressure when considering whether I wish to agree to be in the study.

If I have other questions I should ask the researcher or the research assistant, or contact Research and Sponsored Projects, California State University, Northridge, 18111 Nordhoff Street, Northridge, CA 91330-8232, or phone (818) 677-2901.

X

Signature of Subject

Date
APPENDIX E

SCOPA-COG

Memory and learning

1. *Verbal recall*

Ten words are repeatedly shown for at least 4 seconds, get the patient to read them out loud, the time allowed for recall is unlimited. Underline each word that has been named. When words are named that were not shown, no penalty is given. When a false answer is changed (e.g. king into queen), it is correct.

**Instruction:** "Read the following 10 words aloud and try to remember as many as possible. After reading them all, name as many words as possible, the order of the words is not important".

10 words: Butter arm shore letter queen cabin pole ticket grass engine

(10 correct = 5, 8-9 correct = 4, 6-7 correct = 3, 5 correct = 2, 4 correct = 1, ≤ 3 correct= 0)

score ……../5

2. *Digit span backward*

Ask the patient to repeat a series of numbers backwards; the numbers are read out separately, 1 second per number; if incorrectly repeated, the alternative in the second column is presented. Continue until both the first and the alternative series are repeated incorrectly. Make sure the time interval between numbers stays the same. Read the numbers calmly and make sure the time between numbers is equal. Record the highest series that is repeated correctly at least once; Give an example:

"If I say 2-7-3, than you say (3-7-2)

<table>
<thead>
<tr>
<th>Backwards</th>
<th>score:</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4</td>
<td>5-8</td>
</tr>
<tr>
<td>6-2-9</td>
<td>4-1-5</td>
</tr>
<tr>
<td>3-2-7-9</td>
<td>4-9-6-8</td>
</tr>
<tr>
<td>1-5-2-8-6</td>
<td>6-1-8-4-3</td>
</tr>
<tr>
<td>5-3-9-4-1-8</td>
<td>7-2-4-8-5-6</td>
</tr>
<tr>
<td>8-1-2-9-3-6-5</td>
<td>4-7-3-9-1-2-8</td>
</tr>
<tr>
<td>9-4-3-7-6-2-5-8</td>
<td>7-2-8-1-9-6-5-3</td>
</tr>
</tbody>
</table>

Score……./7
3. **Indicate cubes**

Point to the cubes in the order given below; the patient should copy this; do this slowly; the patient decides for himself with which hand he/she prefers. Indicate the cubes in the order as indicated. Observe carefully if the patient copies the order correctly. When a patient wants to correct a mistake, let him/her do the complete order again. This is not counted as a mistake. However, if the patient forgets the order and would like to see the order a second time, the researcher does not repeat the order again but starts with the next order.

```
■          ■          ■          ■
```

1 2 3 4

a. 1-2-4-2
b. 1-2-3-4-3
c. 3-4-2-1-4
d. 1-4-2-3-4-1
e. 1-4-2-3

Score ……./5

**Attention**

4. **Counting backwards (30 to 0)**

**Instruction**: "Would you subtract three from 30, and subtract three again from the result and continue till zero?". Mistakes can be: the order, missing or not knowing a number, or not finishing off the series. Record the order of numbers named by the patient. If the patient asks where to start or how much to subtract, the researcher
SCOPA-COG

repeats the instructions but counts that as one mistake. If the patient makes a mistake but continues from that point to subtract three, it is only one mistake. If the patient stops the order and starts all over again, it is one mistake.

(0 mistakes = 2, 1 mistake = 1, ≥ 2 mistakes = 0) score ......../2

5. Months backwards

Instruction: "Name the months of the year in reverse order, starting with the last month of the year".

Mistakes are: the order, missing or not knowing the next month, or not finishing off the series. Underline the months that are named correctly. When a month is passed over, this is a mistake, even if the patient corrects it later on. If the patient stops the order and starts all over again, it is one mistake. If the patient starts naming the month forward, repeat the instructions and count it as one mistake.


(0 mistakes = 2, 1 mistake = 1, ≥ 2 mistakes = 0)
	score ......../ 2

Executive functions

6. Fist-edge-palm

1. fist with ulnar side down, 2. stretched fingers with ulnar side down, 3. stretched fingers with palm down; Practice 5 times together with the patient, the patient chooses which hand he/she prefers. Do it slowly and tell the patient to watch carefully and repeat what you are doing. Practice first 5 rounds, with verbal help, e.g. FIST- STRETCH-PALM. Then tell the patient to make the movements alone.

Instructions: “Now it is your turn to make the three movements, fist-stretch-palm, 10 times in a row. You don’t have to count, I will tell you when to stop”.

105
SCOPA-COG

Note the number of correct trios from a total of 10; Count carefully but not out loud. Every time a patient makes a wrong movement, count it as a mistake, even when the patient corrects it halfway.

(10 correct = 3, 9 correct = 2, 8 correct = 1, ≤ 7 correct = 0)

score ……../3

7. Semantic fluency

Tell the patient to name as many animal as he/she knows in one minute. Note all answers that are given by the patient. No repetition or variations of words, such as lion-lioness, tiger-tigress; categories are allowed, bird and pigeon are both correct. Count the number of animals correctly named. The purpose is that the patient generates the animals actively, therefore no clues are allowed. When the patient asks whether, for instance, naming different types of birds is allowed, this may be confirmed. When the patient almost immediately says he/she does not know any more animals, try to stimulate the patient by saying “there is still a lot of time left”, but do not give clues. When the patient starts naming other things than animals, do not correct the patient. Naming other things besides animals is not counted as an additional mistake.

(≥ 25 correct = 6, 20-24 = 5, 15-19 = 4, 10-14 = 3, 5-9 = 2, 1-4 = 1 0=0)

number of animals correct: ……..

score ……../6
Write down all animals named:

8. Dice

Use 2 cards, one with YES = EVEN, NO = ODD; one with YES = HIGHER, NO = LOWER. Put the correct card face up next to the explanation of the test and make sure that the other, irrelevant card is out of sight. The first round (situation 1) is not scored, and the patient is corrected if necessary.

**Situation 1: YES = EVEN**

Put the card “YES=EVEN, NO=ODD” on the table and leave it there during the test. **Instruction:** "Say YES for an even number on a dice and NO for an odd number, when you see a picture of a dice with an EVEN number of pips, I would like you to say YES, and NO when the number of pips is ODD". Show the first two examples (3 even and 3 odd dices) and ask the patient “If you see one of these dice, do you say yes or no?” Tell the patient if the answer is correct or not. If the answer is not correct, explain why. It is important that the patient says YES or NO and not EVEN or ODD. Show the next two examples (with only one dice) and ask the patient “if you see this dice, do you say yes or no?” Tell the patient if the answer is correct or not. If the answer is not correct, explain why. Then show the patient the following 10 dices. Correct the patient if the answer is wrong.
**SCOPA-COG**

**Situation 2: YES = HIGHER**

With the card “example 1” (dice with 3 pips) the next condition starts. Put the card “YES=HIGHER, NO=LOWER” on the table and remove the former card.

**Instruction:** “Now, we change the test a little. When you see a picture of a dice that is higher than the dice on the page before, you say YES. When the dice is lower, you say NO”. Tell the patient you have an example (example 1). “Try to remember this dice” (turn the page) “Is this YES or NO?” Tell the patient whether the answer is correct or not. If the answer is not correct, explain why. Continue with example 2 and say “now remember this dice’(turn the page) “Is this YES or NO?” Tell the patient if the answer is correct or not. If the answer is not correct, explain why.

Then start the test and show all 10 dices one after another. The first response counts and corrections are not allowed. Do NOT correct when a wrong answer is given. If a patient corrects a wrong answer, it is still counted as a mistake. If the patient asks for the instruction, the researcher explains but that is counted as one mistake.

(10 correct = 3, 9 correct = 2, 8 correct = 1, ≤ 7 correct = 0)

number correct: …./10

score ……../3

**Visuo-spatial functions**

9. **Assembling patterns**

The patient is shown 5 incomplete patterns and has to choose 2 or 3 shapes out of 4 to 6 possible alternatives in order to complete the pattern. First practice 2 Figures. Show the patient example A and give the instruction to choose the shapes that form the pattern. Tell the patient if the answer is correct or not. If the answer is not correct, explain why and give the correct solution. Repeat this with example B. Then show the 5 patterns. Do not tell the patient whether the answer is correct or not. There is no time limit. If the patient corrects a wrong answer, this is not counted as a mistake.

a. b. c. d. e.

score ……../5
SCOPA-COG

Memory

10. Delayed recall

**Instruction:** "Can you name as many as possible of the 10 words that you learned during the first test?"

Underline each word that has been named. When words are named that were not shown, no penalty is given. When a false answer is changed (e.g. king into queen), it is correct.

10 words: butter arm shore letter queen cabin pole ticket grass engine

(10 correct = 5, 8-9 correct = 4, 6-7 correct = 3, 5 correct = 2, 4 correct = 1, ≤ 3 correct= 0)

number of correct words: ..../10

score ...../5

Total COG score: ..../43

© This questionnaire is made available free of charge, with the permission of the authors, to all those undertaking non-profit and profit making research. Future users may be requested to share data for psychometric purposes. Use of this questionnaire in studies should be communicated to the developers. No changes may be made to the questionnaire without written permission. Please use the following reference in publications: Marinus J, Visser M, Verwey NA, Verhey FRJ, Middelkoop HAM, Stiggelbout AM, van Hilten JJ. Assessment of cognition in Parkinson’s disease. Neurology 2003;61:1222-1228. For further information, please contact Dr. J. Marinus, Leiden University Medical Center, Department of Neurology (K5Q), P.O. Box 9600, NL-2300 RC Leiden (email: j.marinus@lumc.nl).
APPENDIX F

HEALTH SERVICES RESEARCH UNIT
DEPARTMENT OF PUBLIC HEALTH
UNIVERSITY OF OXFORD

English (USA)

PDQ-39

Parkinson's Disease
Quality of Life Questionnaire
DUE TO HAVING PARKINSON’S DISEASE, how often have you experienced the following, during the last month?

_Due to having Parkinson’s disease, how often during the last month_  
*Please check one box for each question*

<table>
<thead>
<tr>
<th>have you ....</th>
<th>Never</th>
<th>Occasionally</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always or cannot do at all</th>
</tr>
</thead>
</table>

1. **had difficulty doing the leisure activities you would like to do?**  

2. **had difficulty looking after your home, for example, housework, cooking or yardwork?**  

3. **had difficulty carrying grocery bags?**  

4. **had problems walking half mile?**
5. **had problems walking 100 yards (approximately 1 block)?**

6. **had problems getting around the house as easily as you would like?**

7. **had difficulty getting around in public places?**

8. **needed someone else to accompany you when you went out?**

9. **felt frightened or worried about falling in public?**
Due to having Parkinson’s disease, how often during the last month have you .... Please check one box for each question

<table>
<thead>
<tr>
<th>have you ....</th>
<th>Never</th>
<th>Occasionally</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. been confined to the house more than you would like?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>11. had difficulty showering and bathing?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>12. had difficulty dressing?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>13. had difficulty with buttons or shoelaces?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>14. had problems writing clearly?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>
15. had difficulty cutting up your food?

16. had difficulty holding a drink without spilling it?

17. felt depressed?

18. felt isolated and lonely?

19. felt weepy or tearful?

Please check that you have checked one box for each question before going on to the next page.
Due to having Parkinson’s disease, how often during the last month have you ....

<table>
<thead>
<tr>
<th>Question</th>
<th>Never</th>
<th>Occasionally</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>20. felt angry or bitter?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. felt anxious?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. felt worried about your future?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. felt you had to hide your Parkinson’s from people?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24. avoided situations which involve eating or drinking in public?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
25. felt embarrassed in public due to having Parkinson’s disease? □ □ □ □ □ □

26. felt worried about other people’s reaction to you? □ □ □ □ □ □

27. had problems with your close personal relationships? □ □ □ □ □ □

28. lacked the support you needed from your spouse or partner? □ □ □ □ □ □
If you do not have a spouse or Partner, please check here

29. lacked the support you needed from your family or close friends? □ □ □ □ □ □

Please check that you have checked one box for each question before going on to the next page
**Due to having Parkinson’s disease, how often during the last month have you ....**

*Please check one box for each question*

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Occasionally</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>30. unexpectedly fallen asleep during the day?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31. had problems with your concentration, for example when reading or watching TV?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32. felt your memory was failing?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33. had distressing dreams or hallucinations?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>34. had difficulty speaking?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
35. felt unable to communicate effectively? □ □ □ □ □

36. felt ignored by people? □ □ □ □ □

37. had painful muscle cramps or spasms? □ □ □ □ □

38. had aches and pains in your joints or body? □ □ □ □ □

39. felt uncomfortably hot or cold? □ □ □ □ □

Please check that you have checked one box for each question.