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A Longitudinal Study of Fetal Tissue Transplantation Surgery: The Effects on Quality of Life and Personality for Individuals with Parkinson's Disease

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A LONGITUDINAL STUDY OF FETAL TISSUE TRANSPLANTATION SURGERY:
THE EFFECTS ON QUALITY OF LIFE AND PERSONALITY
FOR INDIVIDUALS WITH PARKINSON’S DISEASE

A Dissertation
Presented to
the Morgridge College of Education
University of Denver

In Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy

by
Cynthia C. Cole, M.S.
August 2009
Advisor: Cynthia McRae, Ph.D.
ABSTRACT

Parkinson’s disease (PD) is a chronic and progressive condition that affects the physical, emotional, and social functioning of individuals. Freed et al. (2001) conducted a double-blind sham-controlled trial to investigate the effectiveness of fetal tissue transplantation of those with PD. The authors investigated the effects of the surgery across the dimensions of physical and neurological functioning. A quality of life (QoL) study was conducted to determine if there were differences in QoL when comparing those who received the fetal tissue transplantation to those who received the sham surgery (McRae et al., 2004).

While there is little research on the effectiveness of fetal tissue transplantation as a treatment for PD, there is even less literature on longitudinal effects of this treatment. This study examined the longitudinal trajectory of change in QoL since participants received fetal transplant surgery 10-12 years ago. Participants included 11 people who were in the parent (Freed et al., 2001) and original QoL (McRae, 2004) studies. Participants completed a questionnaire that measured the dimensions of QoL along with a personality inventory, the NEO-FFI. Data gathered from the questionnaires were compared to baseline, one-year, and two-year information on the same participants. Trajectory of change in QoL and personality was assessed with a repeated measures analysis of variance.
For the present study, significant changes over time were found for the Physical functioning ($p < .05$) and Emotional functioning ($p < .10$) dimensions of QoL. A significant result was also found for the Social functioning ($p < .05$) dimension of QoL that was measured by the Social Provisions Scale. In addition, significant results were found for the Neuroticism ($p < .10$), Extraversion ($p < .05$), Openness to Experiences ($p < .05$), and Conscientiousness ($p < .10$) factors of the NEO-FFI. Participants reported a decrease in Physical, Emotional, and Social functioning between the two-year and current assessments. Participants reported an increase in Neuroticism, and a decrease in Extraversion, Openness to Experience, and Conscientiousness between the two-year and current assessments. Findings of the current study provided longitudinal information on the trajectories of fetal tissue transplantation on QoL and personality for participants with PD.
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Chapter One

Introduction

Description of Parkinson’s Disease

Parkinson’s disease (PD) is a neurological disorder that is caused by a dysfunction of the brain. The major symptoms include tremor, slowness in starting and carrying out movements, or bradykinesia, rigidity or muscle stiffness, and difficulties with balance and walking (Jahanshahi & Marsden, 2000). The disease was named after the British doctor, James Parkinson, who first described PD in 1817.

PD affects approximately one in 1,000 people, with incidence increasing as people age. Symptoms develop after the degeneration of at least 80% of dopamine-producing neurons in the substantia nigra (Leader & Leader, 2001). The degeneration of dopamine neurons in the substantia nigra creates substantial physiological disturbances in the basal ganglia, thalamus, and cerebral cortex (Betchen & Kaplitt, 2003). The cause of degeneration in idiopathic PD is not known; however, it is known that the disease is not caused by behaviors, diet, or stress. Except for familial PD, heredity is not believed to be a major cause. It is theorized that certain individuals may have a genetic susceptibility to
developing PD. There are many theories about the cause of PD that are currently under investigation.

PD can be treated and controlled with the appropriate medication for symptoms; however, it does affect activities of daily living and quality of life for individuals who have it. Many people with PD develop dementia, or intellectual decline and loss of memory. Cognitive problems such as absent-mindedness, slower thinking, and difficulty with tasks that require strong mental effort are also common.

Onset and Prevalence

In about 80% of PD cases, the age of onset occurs between the ages of 40 and 70 years old. There is a peak age of disease onset around 60 years of age. It is uncommon for there to be an age of disease onset before 35 years old and after 75 years old in individuals (Leader & Leader, 2001). In young-onset PD, the illness develops between the ages of 21 and 40. Juvenile parkinsonism starts before the age of 21 and is very rare (Jahanshahi & Marsden, 2000).

Although PD progresses slowly, there may be a more intense progression during the first years of the disease. Since levodopa (L-dopa) became the prime treatment for PD in the 1970s, life expectancy for those with PD has been similar to the general population. Individuals with PD are likely to die for the same reasons as the general public, except those with PD are less likely to smoke and ultimately develop cancer (Jahanshahi & Marsden, 2000).
Gender and Ethnicity Differences

Although some studies have stated that men are slightly more likely than women to develop PD, men and women are equally likely to be at risk for the illness (Jahanshahi & Marsden, 2000). The disease affects those from all socioeconomic backgrounds, occupations, and ethnic groups, and is not geographically limited.

Symptoms

There are certain symptoms that are common initial features for those with PD. The first common initial symptom is tremor. The tremor may decrease during periods of sleep and movement, but increases during anxiety. Tremor occurs most often in younger patients. Another common initial symptom is the loss of finger dexterity, which impacts handwriting ability. Decreased movements, such as arm-swinging associated with walking, slowness of gait, reduced volume and monotonous speech are other early symptoms in PD.

In order for a diagnosis of PD to occur, cardinal signs and secondary signs are assessed (Leader & Leader, 2001). The first cardinal sign is tremor while resting. The next cardinal symptom is bradykinesia, or the slowness of initiation of voluntary movement. There is also a reduction in speed and increase in repetition of the movement. Another cardinal symptom is rigidity, or stiffness in the muscles. Degree of rigidity is an important indication of the level of disability for the individual. Another cardinal symptom is akinesia, or the reduction or absence of movement. The last cardinal sign is postural instability, which is a difficulty with balance and walking. Almost all patients
experience bradykinesia and rigidity, while tremor occurs in about 75% of individuals (Leader & Leader, 2001).

Secondary signs are not present during the early phases of PD, but will commonly occur during later stages. These secondary signs include cognitive decline, bradyphrenia (slow thinking), dysphonia (soft, low voice), micrographia (small size of and difficulty with handwriting), loss of facial expression, and dementia. Some psychiatric secondary signs include depression, sleep disturbances, and agitation. Symptoms related to the cranial nerve include decreased eye blinking, blurred vision, or dysphagia (difficulty in swallowing). Autonomic secondary symptoms include orthostatic hypotension, impotence, constipation, sweating, and urinary bladder dysfunction. There may also be sensory symptoms, such as cramps, pain, and olfactory dysfunction. Seborrhea, or excessive greasiness and scaliness of the skin might also occur.

Cardinal, or main symptoms are found in the majority of those with PD. One or more of the cardinal symptoms need to be present in order for a diagnosis of PD to occur. All cardinal and secondary symptoms may not necessarily exist in individuals with PD. In addition, there are individual differences with symptoms across the PD population. For example, there may be differences in the onset of the first symptom, the order and timing of onset of other symptoms, and severity of symptoms (Jahanshahi & Marsden, 2000). The symptoms may also fluctuate in severity according to time of day.

**Drug Treatment**

The main goal of pharmacological treatment of PD is to improve symptoms and quality of life. Although drug treatment cannot alter the history of PD, it is intended to
treat symptoms and more specifically compensate for the deficit in dopamine levels in the brain.

It is debated at which time drug treatment should begin (Leader & Leader, 2001). Some researchers suggest that drug treatment should begin during the early phases of PD to provide an improvement for the individual. Others prefer to wait until motor complications begin. During the absence of drug treatment, psychological, occupational, financial, physiological, and nutritional support may be provided to individuals and their families as they prepare to face the challenges of the disease.

**Surgical Treatment**

Research has led to great improvements in surgical techniques for PD. Surgery may occur for those with advanced PD when drug therapy is no longer effective. In addition to L-dopa being the primary drug treatment for PD, multiple surgical procedures have been used over time to reduce symptoms of the disease.

One early type of surgery for individuals with PD involved surgical lesions to attempt to reduce symptoms of PD. Thalamotomy was the most widely used treatment of this type and was particularly helpful in reducing tremor in PD. Pallidotomy is another type of lesioning surgery that has been used more recently to reduce tremor in PD patients (Côté, Sprinzeles, Elliott, & Kutscher, 2000). Deep brain stimulation (DBS) involves implanting electrodes in the brain to alleviate PD symptoms. The electrodes are attached by wires to a device under the skin in the chest (much like a heart pacemaker) that sends electrical impulses to specific parts of the brain (Côté et al., 2000).
Finally, this study focused specifically on a type of neural transplant surgery, or fetal tissue transplantation for those with PD. The purpose of this surgery was to implant aborted fetal tissue into the caudate and putamen areas of the brain where it was hoped the new tissue would grow and the new neurons would start producing dopamine (Côté, et al., 2000). Unblinded clinical trials have demonstrated that fetal tissue transplantation can improve some symptoms of PD, and that transplanted dopamine neurons may survive (Olanow, Kordower, & Freeman, 1996, Lindvall & Hagell, 2000, Freed et al., 2001, Redmond Jr., 2002, Betchen & Kaplitt, 2003, Björklund et al., 2003). A limited amount of research exists on how fetal tissue transplantation impacts quality of life (McRae et al., 2004) in those with PD.

**Quality of Life**

Although there are very challenging physical symptoms of the disease, PD also affects the physical, social, and emotional aspects of life. The term quality of life (QoL) can include many psychosocial domains. As used in this study, QoL will be used to describe three broad areas: Physical, Emotional, and Social functioning.

The domain of Physical functioning includes the physical aspects of the disease from the patient’s perspective. It considers assessing the ability to perform various activities on and off medications, or when the patient is “best” and “worst.” Standard activities of daily living and stage of disease are also typically included in this domain.

Emotional functioning is a broad area that includes depression, reduced self-esteem, anxiety, and stress. It is not surprising that individuals with PD may become depressed from the physical symptoms alone. It is also possible for depression to be a
side effect of certain drugs. Psychologically, depression may also result from changes in lifestyle and relationships. Anxiety is often common in PD, perhaps resulting from the uncertainties of the disease, or as a result of the disease process itself.

Physical symptoms and motor deficits may become exacerbated by stress. This is because adrenaline, the hormone released when responding to stress, is metabolized by dopamine (Leader & Leader, 2001). Becoming withdrawn after a diagnosis of PD could affect relationships with others, which may ultimately affect self-esteem. Also, sexual problems may result from PD, the drug treatment, or depression. This may greatly impact self-esteem. Other influences on self-esteem may include dwelling on problems, concern over appearance, forgiveness of self and others, and unrealistic expectations of improvement with the disease (Leader & Leader, 2001).

Social functioning is affected in PD patients when movement becomes more difficult and people become more isolated. As symptoms increase, patients find interaction with others becomes more difficult. For example, developing a soft voice, not being able to write, and gradually thinking more slowly all affect abilities to participate in social situations.

Statement of Problem

While there is little research on the effectiveness of fetal tissue transplantation surgery as a treatment for PD, there is even less literature on long-term effects of this treatment. This study examined the longitudinal course of the disease and progress since the surgery of the patients who participated in a fetal transplant surgery trial beginning in 1995. Specifically, the study focused on the QoL aspects of functioning previously
described. This investigation makes a unique contribution to the literature by describing the status of patients who received the implant 10 to 12 years after surgery.

Participants were part of a parent study (Freed et al., 2001) that determined the effectiveness of fetal tissue transplantation. In the parent study, 40 individuals were assessed at Columbia-Presbyterian Medical Center (CPMC) in New York prior to surgery, and at four, eight, and 12 months after surgery. Twenty participants were randomly assigned to receive the fetal tissue transplantation procedure, while the other 20 participants received a sham surgery with the understanding that they could receive the fetal tissue transplantation procedure at a later time. Patients and medical staff were blind to the type of procedure category participants were assigned until 13 months following the surgery. The purpose of the study was to assess whether participants who received the fetal tissue transplantation procedure improved significantly more than those who received the sham surgery, or placebo.

Participants were asked to complete questionnaires assessing QoL immediately following medical evaluations at CPMC (McRae et al., 2004). In addition to QoL data collected before surgery, participants were assessed at four, eight, and 12 months after surgery before the blind was lifted. The purpose of the QoL study was to determine if there were differences in QoL when comparing those who received the fetal tissue transplantation procedure to those who received the sham surgery (McRae et al., 2004).

In the present study, current data on QoL were compared with baseline, one-year, and two-year data on QoL from the original study (McRae et al., 2004). This study assessed longitudinal changes in QoL that occurred over time.
Research Questions

1. What is the trajectory of change in QoL over time for the baseline, one-year, two-year, and current long-term follow-up assessment? Analyses were performed separately on the three original domains of QoL: physical functioning, emotional functioning, and social functioning.

2. Was there any change in personality based on results of the NEO-FFI for the baseline, one-year, two-year, and current long-term follow-up assessment?

Limitations of the Study

Several limitations exist in the present study. First, the sample size is small because it includes only the persons from the original study who participated in the QoL portion of the investigation (n = 30). Of that number, some participants in the original sham surgery group did not receive the transplant, some participants had passed away, while others were either not able to be located due to outdated contact information or were not interested in participating in the current study. The total number of participants who were involved in the present study was small (n = 11).

Second, the results from this study cannot be generalized to other individuals with PD. This was a very unique study that involved experimental surgery and included the condition of sham brain surgery. In addition, the double-blind lasted more than one year. Individuals who volunteered for this investigation were truly pioneers and the results of the study provided important information about who received the best results from the surgery and how long the effects have lasted.
Summary

Chapter One presented an introductory synopsis of PD, including the physiology, onset, symptoms, drug and surgical treatment, and QoL. In Chapter Two, a review of the literature will present more detailed information on PD, drug treatments, surgical interventions, fetal tissue transplantation, long-term progression of PD, and QoL.
Chapter Two

Literature Review

Introduction

Chapter Two provides a literature review on various aspects of PD. Topics include a more extensive introduction to PD, additional information on drug treatments and surgical interventions, with a focus on fetal tissue transplantation, long-term progression of PD, and QoL.

The literature reviewed in this chapter was retrieved in numerous ways. First, a computer search using the database MEDLINE was used to identify literature pertaining to this study. Search topics included QoL, surgical treatment of PD, fetal tissue transplantation surgery, drug treatment of PD, and history of PD. A secondary search utilized the databases Academic Search Premier, PsycINFO, and PsycARTICLES. Search topics included QoL, PD, and treatment of PD. Books were located from libraries that included information on PD and QoL. In addition, authors and titles were identified from reference lists that were relevant to the study.

Definition of PD

Since its original description by James Parkinson, PD has been considered the prototypic movement disorder (Rascol et al., 2003). PD is a degenerative neurological disorder that has a considerable impact on the physical, emotional, and social aspects of
patients’ lives. A diagnosis of PD generally relies on the observation of the principal symptoms: tremor, rigidity, balance impairment or postural instability, bradykinesia (slowness of movement), and dyskinesia (abnormal involuntary movements and postures). Although patients may have different levels of these motor symptoms, patients are typically diagnosed with PD when there is a presence of one or more of these symptoms (Stacey & Jankovic, 1992).

PD is primarily a movement disorder; however, it also severely impacts the autonomic, cognitive, and psychiatric functions of individuals. The impairment on these “non-motor” systems can adversely harm individuals with PD while strongly impacting their QoL. Non-motor symptoms tend to be unresponsive to antiparkinsonian medication, and may even be worsened by this treatment. The cause of PD is unknown, but evidence has suggested that environmental and genetic factors may at least contribute to the cause of the disease (Guttmen, Kish, & Furukawa, 2003). PD is associated with a degeneration of nigrostriatal dopamine neurons in the brain, yet the degeneration may also impact other central and peripheral areas of the nervous system (Rascol et al., 2003).

Progression of PD often includes an increase in difficulty with mobility, balance and speech, and non-motor symptoms, including cognitive decline and depression (Keränen et al., 2003). “Off” phases are periods of increased PD disability, while “on” phases are periods of little or no PD-related motor disability (Hagell et al., 2002).

The disease affects 1% of the population over the age of 60 (Firbank, Burn, McKeith, & O’Brien, 2005). Although many important advances have led to a better understanding of the underlying pathophysiology of PD, no treatments have been developed which cure the disease (Guttmen et al., 2003). Because the presentation of PD
varies among patients, most clinicians follow the course of each patient and make
decisions for treatment according to the individual needs of each person.

According to Rascol et al. (2003), there are factors that contribute to optimal
treatment of PD. Treatment should be efficacious in reducing PD symptoms while
slowing down rate of disease progression and increasing life expectancy. Treatment
should also work while limiting the development of adverse side effects. Finally,
treatment should be cost effective while also being available to all patients, regardless of
social or economic status.

**Drug Treatment of PD**

Levodopa (L-dopa) is the most effective medication for the treatment of PD
symptoms. This medication acts as a replacement therapy for the dopamine deficiency
caused by PD. All patients with PD will utilize L-dopa in their treatment at some time
during the progression of the disease. L-dopa is most efficacious during the first years of
treatment. This period of treatment is known as the L-dopa “honeymoon” (Rascol et al.,
2003). Long-term use of L-dopa and other pharmacological treatments results in a decline
of effectiveness of the medications over time. Thus, the limitations of L-dopa become
more prominent during the more advanced stages of PD. Some limitations of L-dopa
include a lack of improvement for many disabling motor and non-motor PD symptoms,
side effects, and the inability to stop the progression of PD (Rascol et al., 2003).

The benefits of L-dopa may be outweighed by motor complications caused by the
drug, including fluctuations and dyskinesias. The Parkinson Study Group (2004)
designed a study to evaluate the effects of L-dopa on the progression of PD. In this study,
361 who never had received dopaminergic drugs were randomly assigned to placebo or L-dopa at 150, 300, or 600 mg/day for 40 weeks, which was then followed by a 2 week period off the drugs. Scores from the Unified Parkinson’s Disease Rating Scale (UPDRS) showed an increase (higher level of depression) in 7.8 points for the placebo group. The two lowest doses of L-dopa had an increase of 1.9 points, and there was a decrease in 1.4 points for the highest dosage group. Freezing was observed in the placebo group, but dyskinesias were commonly found in the highest dosage group (The Parkinson Study Group, 2004).

Jankovic (2006) stated that the emergence of dyskinesias due to L-dopa may be related to the shortening of L-dopa’s half-life in the striatum because the body with PD has an impaired ability to store the L-dopa due to the loss of dopamine terminals. Since this is occurring, there is less of a continuous delivery of L-dopa to the brain. The recommendations for reducing L-dopa induced dyskinesia is to reduce each dosage of L-dopa, use drugs that are known to reduce dyskinesias, and to get surgery.

**Surgical Treatment of PD**

The ultimate decline of effectiveness of drug therapy has led to an exploration of alternative treatment for PD symptoms (Clarkson & Freed, 1999). Freed et al. (2001) reported that although L-dopa was the treatment of choice for years, motor fluctuations such as bradykinesia and hyperkinesias still developed in many patients with PD over time. No drug therapies have proven to effectively improve motor fluctuation for extended periods of time. Therefore, several types of surgery were developed as
alternative treatments of PD. These treatments include ablative surgeries, deep brain stimulation, gene therapy, and neural transplantation.

**Ablative Surgery**

Surgical procedures were common for those with PD in the 1950s and '60s. When L-dopa was developed, surgery became a less popular treatment method. Researchers in Sweden and France started experimenting with surgery again during the 1980s, and American physicians did the same in the early 1990s (Cowley, Murr, Peyser, & Sawhill, 2000). Before modern surgeries evolved, ablative surgeries were the popular method of surgery for PD.

In ablative surgery, brain tissue affected by PD is located and then destroyed. The purpose of the procedure is to remove tissue that produces abnormal chemical or electrical impulses that will ultimately create tremors and dyskinesias. The two types of ablative surgery are thalamotomy and pallidotomy.

The first type of ablative surgery that was used was thalamotomy. During this surgical procedure, part of the thalamus is destroyed (Cowley et al., 2000). Thalamotomy is primarily used to eliminate tremors. During a thalamotomy procedure, part of the tissue in the globus pallidus is destroyed. Typically, pallidotomy is performed to eliminate uncontrolled dyskinesias. When surgery on both sides of the brain is performed, side effects such as weakness and slurred speech may occur. Therefore, one side of the brain is typically targeted in the operation (Cowley et al., 2000).

Comparing research findings of thalamotomy and pallidotomy procedures is difficult because of the variation in the areas targeted, the surgical procedure, selection of
patients, and rating scales (Krack & Vercueil, 2001). Thalamotomy has been found to improve symptoms of dystonia, a condition where muscle contractions often cause twisting and repetitive movements. Some researchers have found that the amount and severity of complications, mainly speech disturbance, is at a lower rate after pallidotomy, rather than thalamotomy (Krack & Vercueil, 2001).

Deep Brain Stimulation (DBS)

Researchers have found that the subthalamic nucleus (STN) and the globus pallidum internus (GPI) areas of the brain play an active role in the symptoms of PD (Jankovic, 2006). During deep brain stimulation (DBS) surgery, electrodes are implanted in the brain (Krack et al., 2003). A few days after implantation of the electrodes, a generator or pacemaker is implanted in the chest and adjusted to the correct settings. The areas of the brain with electrodes are then targeted with high frequency stimulation to reduce PD symptoms. High-frequency DBS simulates the effect of a lesion without deliberately damaging the brain (The Deep-Brain Stimulation for Parkinson's Disease Study Group, 2001).

Several studies have shown that DBS of the GPI and STN can improve symptoms of PD and prolong the “on” time (Jankovic, 2006). In a double-blind study of 143 patients with advanced PD, DBS was performed. Results indicated that motor scores of the treatment group improved by 49% when compared to the group who did not receive DBS. Six months after receiving the procedure, “on” time without dyskinesias for those receiving DBS of the STN had improved from 27 to 74 percent. Those who had received DBS of the GPI had an improvement from 28 to 64 percent (Jankovic, 2006). Adverse
side effects included intracranial hemorrhage in seven participants and lead explantation in two patients. Speech did not improve over time. The authors concluded that STN DBS is not better than L-dopa, but that it does improve motor complications related to taking L-dopa, and dyskinesias and off-period dystonia (Jankovic, 2006).

Krack et al. (2003) studied 49 patients with PD for 5 years following DBS. The participants were assessed at 1, 3, and 5 years with L-dopa (on medication) and without L-dopa. After five years, the researchers found significant improvement in motor symptoms and dystonia while off L-dopa, and in dyskinesia while on medication. The study did not include a control group. Consistent with the long-term progression of PD, the researchers found that there was an increase in akinesia and freezing of gait, and a decline in speech, postural stability, and cognitive functioning (Krack et al., 2003).

Gene Therapy

Gene therapy has long been considered as a treatment option for PD. Gene therapy includes adding a gene into cells with the goal being to change the functioning of these cells (Betchen & Kaplitt, 2003). A second type of gene therapy includes placing the gene under a regulatory control that will initiate a production of the gene in cell locations that do not normally reproduce the gene (Betchen & Kaplitt, 2003). The ultimate goal of these gene therapy procedures is to genetically change the functioning of neurons in the brain. Research into gene therapy is ongoing, but science in this area has not progressed to the point of applying the research to human candidates.
Neural Transplantation

During the neural transplantation procedure for PD, the goal is to transplant or replace the dopamine producing neurons of the substantia nigra that are impaired (Betchen & Kaplitt, 2003). Examples of neural transplantation include stem cell transplantation and fetal tissue transplantation.

Neural Transplantation: Stem Cell Transplantation Surgery

Stem cells are immature cells that have an ability to self-renew, depending on site of origination. They also have the ability to differentiate into multiple cell types (Lindvall, Kokaia, & Martinez-Serrano, 2004). Even though animal studies have shown that stem cells survive four times longer than fetal cells, only 22% of grafted stem cells in one study survived (Kawasaki et al., 2000). A small fraction of the 22% of cells actually produced dopamine.

The results of randomized trials of implanting stem cells for those suffering from PD have generally been disappointing (Rice, Halfpenny, & Scolding, 2003). If the procedure were proven to be an effective form of treatment for PD, there are certain criteria that should be further explored. For example, there needs to be a more clear definition of the method for selecting patients appropriate for this type of therapy. Also, there needs to be an improvement in the efficacy of grafts. There is no evidence that stem-cell neurons will create a more pronounced improvement over fetal neuron grafts. Lastly, there needs to be more research on adverse side effects on this type of therapy (Lindvall et al., 2004). Stem cell therapy is considered a promising yet controversial type
of treatment for neurodegenerative disorders. Social issues surrounding this practice influence the pace of scientific discovery on the efficacy of this procedure.

**Neural Transplantation: Fetal Tissue Transplantation Surgery**

It was believed that fetal tissue transplantation could improve motor fluctuation in patients where the levodopa had become inefficient in treating the disease (Freed et al., 2001). Clinical trials in the mid to late 1980’s showed that fetal tissue transplantation surgery had the ability to reduce some PD symptoms, and that transplanted neurons can survive (Freed et al., 2001). Because the present study is based on fetal tissue transplantation surgery, the focus of the remainder of this introduction and the literature review will be specifically on this treatment.

Advances in interventions in PD treatment depend on technology and expertise, thus making them costly. In order for these interventions to gain acceptance in the scientific community, it is important that they demonstrate long-term effectiveness beyond the successes of current treatments for PD. Effective treatment of PD will ideally address the nature of PD symptoms themselves, but also the social and emotional consequences of the disease (Hjelmgren et al., 2006).

Since 1988, patients with PD have been involved in clinical trials investigating the efficacy of neural transplantation of fetal tissue into the brains of those affected with the disorder (Clarkson & Freed, 1999). Fetal tissue transplantation surgery has been used as an experimental procedure to reduce symptoms of PD (Bethche, & Kaplitt, 2003; Freed, Greene, & Breeze, 2001). This type of surgery includes the stereotactic implantation of human embryonic dopamine neurons into brain tissue of those suffering
from PD (Freed et al., 2001). The premise of this surgery is based on the belief that dopamine-producing tissue from fetuses within a six to ten week gestation period will produce positive results for the recipient. This includes reinnervating the striatum by establishing dendritic connections with the already existing dopamine receptors (Freed et al., 2001).

The efficacy of fetal tissue transplantation surgery for reducing the symptoms in individuals with PD has been investigated (Freed et al., 1992; Clarkson & Freed, 1999; Clarkson, 2001). Freed et al. (1992) initially used the implantation of dopamine cells in seven individuals with PD. Improvements in motor symptoms and functioning were reported following the procedure. However, questions remained regarding the experimental nature of the procedure and the influence of a placebo effect on the positive outcome of the surgeries (i.e., placebo effect and a lack of a comparison group). Clarkson (2001) reviewed the fetal tissue transplantation literature, and summarized that even though this treatment has led to a reduction in levodopa administration and an improvement in motor skills, several questions need to be addressed regarding this procedure before it can become more widely accepted.

Clarkson and Freed (1999) found that the transplantation resulted in patients requiring less L-dopa administration and a moderate improvement in motor skills. Olanow et al. (2003) studied 34 patients with PD during a 24-month double-blind, placebo-controlled trial of fetal transplantation. There was no significant improvement in the treatment group when compared to the control group. They did find a significant benefit in the transplant when the patients had less severe motor symptoms at baseline.
This result suggests that the procedure prevented further deterioration of motor symptoms, rather than an improvement in motor symptoms (Olanow et al., 2003).

Freed et al. (2001) studied patients with PD who received transplantation of human embryonic dopamine neurons. The results indicated that the neural tissue survived in those who had a severe form of PD. It was noted that more clinical benefit was found in younger patients than older patients.

Results of the Parent Fetal Tissue Transplantation Study

Freed et al. (2001) conducted a double-blind sham-controlled trial to investigate the effectiveness of fetal tissue transplantation (human embryonic dopamine neurons) into the brains of those with advanced PD. Specifically, the authors investigated the effects of the surgery across the dimensions of physical and neurological functioning. The purpose of the study was to determine whether those in the transplant group experienced more improvement than those in the sham group over the one year period of the double-blind.

The fetal transplantation surgery that occurred in the parent study (Freed et al., 2001) included the following procedural steps. All 40 participants had a stereotactic frame attached to their head for magnetic resonance imaging for the purpose of deciding the location of the needle tracks for the tissue implantation (McRae et al., 2004). Four burr holes were drilled bilaterally into the foreheads for the needles while the participants were awake. Scalp incisions and twist drill holes occurred while the participants were under local anesthesia. Both the transplant and sham participants received the same preoperative evaluation, sedation, and pain control. Implants into the putamen with
embryonic mesencephalic tissue containing dopamine neurons occurred for those in the transplant group. Those receiving the sham surgery had needles that were empty and did not penetrate the brain (McRae et al., 2004). Additional information about the surgical procedure can be found in the parent study article by Freed et al. (2001).

Participants included a volunteer sample of 40 individuals with idiopathic PD; 20 persons received the transplant and 20 persons received the sham surgery with the option of receiving the transplant after one year when the blind was lifted. Thirty participants volunteered for the QoL study. Of these 30 participants, 12 received the transplant, and 18 received the sham surgery. Assessment of QoL was done at baseline, four, eight, and 12 months after surgery (McRae et al., 2004).

**Results of the Original QoL Study**

McRae et al. (2004) investigated QoL and medical outcomes of the transplant and sham surgery groups at 12 months before the double-blind was lifted. In addition, the QoL study examined perceived treatment groups at four, eight, and 12 months in terms of QoL and medical outcomes. The investigators found only two changes over time among those who received the transplant. However, according to the participants’ perceived treatment, there were many changes within the one year of the double-blind condition. Participants who believed they had received the transplant reported more positive results regarding QoL than those who thought they had received the sham surgery. The authors also included ratings by the medical staff, which produced the same result. Results indicated that the placebo effect was very strong in this placebo-controlled surgical trial.
Research regarding fetal tissue transplantation as a treatment for the improvement of PD symptoms has been inconclusive. Investigation of this intervention was discontinued at the end of the federal funding by the National Institute of Health in 2001.

**Longitudinal Follow-up of 10-12 Years After Original Study**

In the present study the longitudinal effects of fetal tissue transplantation surgery on QoL factors for patients suffering from PD were investigated. The participants were the same individuals who were involved in the original QoL study (McRae et al., 2004). These patients received the surgery between 1995 and 1998 and were followed until 2000 (Freed et al., 2001). Those participants receiving the sham surgery were later offered the transplantation surgery, and were, therefore, potential candidates for this follow-up study. The purpose of this study was to investigate the long-term effects of the fetal transplant surgery on these individuals, specifically looking at QoL. Present QoL and changes over time in terms of QoL were investigated. Measures focused on the three dimensions of QoL: Physical, Emotional, and Social functioning. These data were collected 10-12 years after the surgery took place to determine longitudinal effects of the transplant. The current data were compared to the baseline, one-year, and two-year data from the original study (McRae et al., 2004). By doing this comparison, changes over time were investigated.

**Importance of Study**

**Unique Sample**

Longitudinal studies pertaining to the topic of fetal tissue transplantation and PD have not been done, and a follow-up investigation will be important to study the changes
in QoL that these participants have experienced over time. A longitudinal investigation of the effects of this surgery will be an important contribution to this field of literature.

**Quality of Life**

Quality of life (QoL), as defined in this study, includes three aspects: Physical, Emotional, and Social functioning. By studying QoL, there is an intimate look at how the surgery has impacted the participants on an everyday basis. Components of QoL include how participants view their health, performance of daily activities, severity of symptoms, description of feelings, levels of stress, level of social support, and interaction with others. An important method in promoting patients’ point of view in clinical practice and decision processes is discovered by investigating QoL (Bergland & Narum, 2007).

QoL more specifically may describe people’s sense of well-being, purpose in life, autonomy, identification with certain roles, and ability to participate in significant relationships. Factors of QoL that face people with PD may also include symptoms and needs of a changing physical body, difficulty with communication, unpredictability of the disease, and a changing sense of identity (Koplas et al., 1999). Individuals with a chronic disease like PD may also struggle with their sense of control. Perception of control is also related to sense of well-being and adjustment to having PD. One study found that the patient’s perceived control of symptoms of PD was significantly related to patient and caregiver well-being (Wallhagen & Brod, 1997). Koplas et al. (1999) found that PD patients’ beliefs that their behavior could influence the outcome of personal situations and life events was a significant predictor of QoL. This perceived control factor was a
large influence on QoL, even though the participants may have been experiencing depression and physical disabilities.

Knowledge of QoL and its influence is important when managing a serious disease like PD. Although there is no known cure for PD, there is a relatively normal life expectancy with modern treatments available (The Global Parkinson’s Disease [GPDS] Steering Committee, 2001). Both PD symptoms and medications greatly influence QoL. Depression and cognitive impairment have also been found to be significant predictors of QoL when dealing with PD (GPDS, 2001).

Reuther et al. (2007) assessed QoL in 145 individuals with PD during a 12 month period by using a non-disease specific and also disease-specific QoL scales. Significant changes in QoL were found in the disease-specific QoL scales, but not the general assessments. The disease-specific scales were sensitive to changes in QoL, revealing that PD considerably affected QoL over the 12-month period. Specifically, the presence of depression, motor complications, falls and gait instability, type of PD, and cognitive impairment were identified as predictors of QoL. The authors concluded that future studies are needed to specifically evaluate QoL changes over long periods of time.

Kuopio, Marttila, Helenius, Toivonen, and Rinne (2000) examined QoL in 228 patients with PD. They investigated the associations of age, age at onset, duration, clinical stage, depression, and dementia. The authors found that depression was more commonly found among female patients with PD. They also found that as PD progressed, there was a decrease in QoL on the dimensions of Physical functioning, role limitations, and Social functioning. Longer duration of illness was related to diminished Social functioning. The older the patient was at the onset of the disease, the lower the QoL in
Quality of Life and Depression

Due to diagnostic and selection criteria, there are varying degrees of reported prevalence of depression in those with PD. Based on a general consensus, depression affects approximately 40% of those with PD and greatly impacts QoL (Rascol et al., 2003). There is not a linear relationship between degree of depression and severity of PD symptoms. Depression is more commonly found in patients who are at the initial and later stages of PD (Cummings & Masterman, 1999).

Depression may occur more often in those with PD than among the general population. Early onset of PD symptoms (before 55 years) and a family history of PD are common risk factors for depression in PD. There may be a positive clinical response to antidepressant medication among those with PD (Cummings & Masterman, 1999). Neurologists of the Parkinson’s Study Groups (PSG) care for over 20,000 patients with PD. A survey 49 neurologists revealed that only 26% of PD patients were receiving antidepressant medication for depression (Cummings & Masterman, 1999). Controlled trials to better understand pharmacological treatment of depression for those with PD have not yet occurred (Guttman et al., 2003).

Other psychiatric symptoms may also occur in PD patients. For example, drug induced psychosis may be a management problem and could potentially create difficulty for families providing care to those with PD at home. Other symptoms that could develop
include visual hallucinations, paranoia, and other psychotic symptoms (Guttman et al., 2003).

**Quality of Life and Anxiety**

Similar to those without PD, anxiety has a negative effect on QoL for those with PD. Anxiety has been related to increased psychosocial disability (e.g., activities of daily living) and decreased sense of emotional well-being in those suffering from PD. Nearly 40% of individuals with PD meet a diagnosis for anxiety disorders (e.g., generalized anxiety disorder, panic disorder, and social phobia) in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Menza & Dobkin, 2005).

Individuals with PD often experience anxiety prior to the onset of PD. The anxiety often is comorbid with depression and becomes more severe when motor fluctuations develop. Those with PD most likely also experience anxiety due to the neurochemical and degenerative changes that occur within PD, in addition to the debilitating progression of PD. Anxiety has been found to be a stronger predictor of QoL than either physical symptoms or major depressive disorder in the areas of interpersonal interaction quality, health satisfaction, and overall well-being (Menza & Dobkin, 2005).

Studies have shown that there is often a comorbidity of depression and anxiety for those with PD. The impact of comorbid anxiety and depression on treatment and progression of PD remains unknown. Some have stated that comorbid depression and anxiety with PD is correlated with greater chronicity, treatment resistance, and a worse prognosis (Brooks & Doder, 2001). Research has shown that there was an increased
comorbidity of non-motor symptoms such as depression and anxiety connected with more severity of PD symptoms (Shulman, Taback, Rabinstein, & Weiner, 2002).

**Quality of Life and Cognitive Decline**

Although many symptoms of PD are related to physical ability, the disease also affects intellectual functioning. Most people with PD will be affected by cognitive impairment. Symptoms of cognitive decline include attention difficulties, concentration, problem solving, and memory. These areas of decline often are reported in relation to paying attention at work, difficulty handling more than one project at a time, difficulty with planning and organizing responsibilities at home, and problems with completing tasks after they have begun (Bassett, 2005).

A significant number of people will develop dementia during the course of PD. A recent study suggested that 20% to 40% of those with PD will eventually develop dementia, with a 10% incidence rate per year (Aarsland, Andersen, Larsen, Lolk, & Kragh-Sorensen, 2003). Menza and Dobkin (2005) stated there is a relationship between anxiety and cognitive impairment among both non-PD and PD individuals.

**Important Patient Data on Quality of Life**

It was important to assess how QoL has improved, worsened, or stayed the same for individuals who received the fetal tissue transplant surgery. The data gathered were compared to data from baseline, one-year, and two-years after surgery from the original study (McRae et al., 2004) to determine how QoL had changed over time. This study is important because it provided information related to whether or not this procedure was viable or was helpful for any of the previous participants. Results of this project will
contribute to the body of knowledge related to which types of patients, if any, might potentially benefit most from the surgery. The study also determined the length of time that the effects of surgery have lasted. Thus, results of the investigation provided information on whether the fetal tissue transplantation surgery is a useful procedure to pursue, and how it might be a credible alternative treatment for some people.

Guidelines for Future Transplant Studies

The results of this study were valuable in gaining longitudinal data on the effects of fetal tissue transplantation for PD. Another benefit of this study is that it makes important inferences regarding the effectiveness of the surgical procedure. This includes how the patients responded to the surgery, and how well the surgery worked for each patient. By gathering these data, it is hoped that the results indicated who has benefited the most, the least, or not at all from the transplant surgery. Results may suggest selection criteria for those with PD who may consider this type of surgical treatment.

Longitudinal Research and Progression of PD

Knowledge about the expected progression and outcome of treatment are beneficial for the knowledge of any disease. Primary goals of health psychology include a thorough description and explanation of changes over time with disease (Hagell et al., 2002). Longitudinal studies can reveal the comprehensive evidence of progress, stagnation, or decline (Hagell et al., 2002). By studying longitudinal data, researchers can better understand which factors contribute to the improvement or progression of a disease (Rosser & Dunnett, 2003). This type of research may also be valuable in determining which aspects of disease are specifically improving or declining over time. This
knowledge also contributes to a better facilitation for treatment and long-term change. Long-term follow-up studies provide an increase in knowledge that may ultimately contribute to the planning of rehabilitation for disease.

**Long-Term Change in Parkinson’s Disease**

PD is a degenerative neurological disorder that includes a slow deterioration in the QoL of those afflicted with the disorder. It is a progressive condition that worsens over time. Although the rate of nigral cell death is not known, neuroimaging techniques estimate that the rate of cell death occurs approximately 10% every year (Rascol et al., 2003).

Longitudinal studies of PD have focused on cognitive, medical, and functional changes over time. Even without dementia, PD can have a harmful impact on cognitive decline. Azuma et al. (2003) reported that significant cognitive impairment may be observed for eight years and longer, but cognitive decline is slower over briefer periods of time, such as one year. Comparing control elderly individuals to those with PD can demonstrate deficits in relative performance, but longitudinal data can provide knowledge on how cognitive processes change over long periods of time (Azuma et al., 2003).

Jacobs et al. (1995) studied the factors that predict cognitive decline in individuals with PD. Neuropsychological tests were administered to 111 PD patients who did not have dementia. There were 23 patients who were diagnosed with dementia at follow-up testing (2.7 years). Factors associated with dementia included age, Unified Parkinson’s Disease Rating Scale (UPDRS) scores, and depression. Mahieux et al. (1998) found that
among the 81 non-demented PD patients, 19 were diagnosed with dementia at follow-up testing. The researchers found that Picture Completion from the WAIS-R and age of disease onset were significantly related to dementia. Azuma et al. (2003) tested PD patients twice across two years and found cognitive decline across disease progression.

One reason to study the longitudinal effects of fetal tissue transplantation on PD is to differentiate the results compared to the normal progression of PD without this surgical procedure. Rosser and Dunnett (2003) expected the benefits of fetal tissue transplantation to not be detectable in PD patients for at least a year, based on animal studies and current research on PD patients. Piccini et al. (1999) reported that PD studies show that it may take subsequent years post-neural transplantation surgery to see the beneficial effects.

Hagell et al. (2002) studied dyskinesias following fetal tissue transplantation in Parkinson’s disease. The authors retrospectively studied 14 patients 11 years after receiving fetal tissue transplantation. They found that dyskinesias (abnormal involuntary movements and postures) increased during postoperative off phases, but were generally of mild to moderate severity. They concluded that off-phase dyskinesias probably did not result from excessive growth of grafted dopaminergic neurons.

Management of PD is intended to improve the QoL of patients. Drug therapy is only one of the options for the management of PD. Different medical therapies are utilized according to the symptoms and stages of patients’ disease. The primary goal of management is for the patient to have as close to normal functioning as possible with the absence of side effects from the therapy (Rascol et al., 2003).
Quality of Life: The Importance of the Patient’s View in Clinical Trials

It is important to include patients’ perspectives of the impact of PD and its treatment on their QoL. Patients have been involved in evaluating different aspect of health care at an increasing rate (Staniszewska, 1999). Traditional medical ways of collecting health information, such as laboratory tests, can be limiting in the type of information provided. For example, a radiological test will not give information regarding patients’ reactions or emotions about their illness. Patient perspectives, or QoL information is now considered to be central in the treatment of chronic disease (Staniszewska, 1999).

QoL encompasses a person’s physical health, psychological state, personal beliefs, social relationships, and relation to features in the environment (Calvert & Freemantle, 2003). It also includes the manner in which disease and treatment affect emotional, physical, and social well-being. QoL serves as a subjective indication of the individual’s perception of the impact of disease and treatment on health status (Calvert & Freemantle, 2003).

Research on disease has mainly focused on symptoms, survival, and treatment, for example. Although these outcomes play an instrumental role in understanding chronic disease, it is also important to better understand the effect the disease has on everyday activities, mobility, and relationships. QoL measures have been developed to assess patients’ perspectives of their health and well-being on a subjective level (Staniszewska, 1999). Understanding QoL can enable physicians and those on the treatment team to gain knowledge of how patients are coping with the progression of the disease. Information from patients can also provide clinicians with knowledge that can help other patients
dealing with the same issues related to treatment (Calvert & Freemantle, 2003). QoL as a component of health treatment has been emphasized in studies where patients and clinicians provide different interpretations of care, indicating that ideas from both sides should be considered in treatment. Improving QoL is vital when dealing with a chronic illness like PD, a disease that cannot be cured, but must be endured for years.

A long-term follow-up to treatment that is focused on QoL of the patient should explore the patient’s values and treatment effects that are meaningful to the individual. In addition, it is important to examine the patient’s understanding of PD, evaluations, treatment decisions, and possible outcomes (Sweet, 2004). The measure of QoL should allow each participant to provide their personal assessment of change over time (Paterson, 2004). These subjective health questions enable patients to contribute to evaluating outcome, and to have the importance of helping follow-up research findings to be more patient-centered and relevant (Paterson, 2004). It is rare for follow-up studies to capture patients’ perspectives of change. However, it is the aim of this study to do just that.

Summary

Chapter Two provided a literature review on detailed information on PD, drug treatments, surgical interventions, fetal tissue transplantation, long-term progression of PD, and QoL with PD.

PD is a chronic and life-altering disorder that affects many individuals, mainly during the later stages in their lives. Although much literature exists on the nature of PD, and drug and surgical treatments, there is minimal research on the QoL for these individuals, especially over an extended period of time. More specifically, little is known
about the QoL of those who received fetal tissue transplantation surgery as a method to reduce PD symptoms.

The present study was designed to investigate the QoL for participants who received fetal tissue transplantation in the parent study 10-12 years ago. The study assessed how individuals’ Physical, Emotional, and Social well-being has changed over time since the initial surgery.

Chapter Three will discuss the method and procedure used in this study while investigating longitudinal changes in QoL and PD.
Chapter Three

Method

Chapter Three describes the methodology used in the present study. This chapter includes information on the participants, measures, and data analyses.

Participants in Parent Parkinson’s Disease Study

Patients were recruited for the parent study (Freed et al., 2001) through contacts with neurologists across the United States and Canada, and in consultation with Dr. Stanley Fahn (Columbia Presbyterian Medical Center; CPMC) and Dr. Curt Freed (University of Colorado Health Sciences Center; UCHSC). Patients were assessed and evaluated two times for three or four days at each time before being accepted into the parent study. For the parent study, there were 40 patients who were accepted as participants.

Participants in Original Quality of Life Study and Current Investigation

Of the 40 patients in the parent study, 30 of them agreed to participate in the original QoL study. Of these 30 participants from the original study, updated contact information was identified for 14 people. For the remaining 16 participants, either contact information was unable to be found, some people refused to participate, or some participants had passed away. Of the 14 participants, 11 of them agreed to participate in the current investigation. Demographic information for the participants involved in the
current study is presented in Table 1. For the demographic variables of age, duration of
disease, and duration of education completed, data were collected from the baseline
assessment. For the demographic variables of current living situation, marital status,
currently paid for employment, and volunteer work, data were collected from the current
assessment. The demographic variables gender and ethnicity remained the same.
Table 1

Demographic Information of Participants in the Current Investigation

<table>
<thead>
<tr>
<th>Demographic Variables</th>
<th>Demographic Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: Male</td>
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<tr>
<td>Female</td>
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<tr>
<td>Age (from baseline assessment)</td>
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<td>Mean years</td>
<td>51.91 ± 7.53</td>
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<tr>
<td>Range</td>
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<tr>
<td>Duration of disease (from baseline assessment)</td>
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<td>Mean years</td>
<td>13.64 ± 4.95</td>
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<td>Range</td>
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</tr>
<tr>
<td>Other</td>
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</tr>
<tr>
<td>Duration of education completed (from baseline assessment)</td>
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<tr>
<td>Mean years</td>
<td>16.82 ± 2.27</td>
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<tr>
<td>Range</td>
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<td>Current living situation - number (from current assessment)</td>
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<tr>
<td>Living in residential setting</td>
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<td>Marital Status - number (from current assessment)</td>
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<td>Currently paid for employment (from current assessment)</td>
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<td>Volunteer work (from current assessment)</td>
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<tr>
<td>Yes</td>
<td>6</td>
</tr>
<tr>
<td>Previously, but not currently</td>
<td>2</td>
</tr>
</tbody>
</table>
Inclusion and Exclusion Criteria

There were several inclusion criteria that needed to be met in order for participants to be accepted into the parent study (Freed et al., 2001). The participants needed to be in an advanced stage of idiopathic PD for at least seven years with some responsiveness to L-dopa. Another criteria was that there needed to be a continued yet reduced improvement from the L-dopa treatment. The patients had previously tried other forms of medical treatment, and were now medically appropriate to undergo transplant surgery with certification by their physicians. There was evidence of chronic symptoms, such as “off” periods and dyskinesias or freezing which were not controlled by dopamine medication. The participants were willing to participate in ongoing research, and were able to pay for expenses not covered by the initial NIH grant for the parent and original studies. In addition, the participants fell in the age range of 20 to 75 years, and had no serious depression, hallucinations, or cognitive impairment. Finally, the participants had normal MRI brain scans within the last 18 months of the parent and original studies, and their PET scans were indicative of idiopathic PD (Freed et al., 2001).

Exclusion criteria for participants in the parent and original studies included severe or moderately severe depression, gross signs of dementia, and previous brain surgery or injury. Additionally, participants could not show evidence of diabetes, severe cardiopulmonary disease, other severe medical conditions, or MRI evidence of a cerebrovascular disease. Patients who could not get medical clearance from their physicians were not accepted to participate in the transplant study (Freed et al., 2001).
Procedure

The same participants accepted into the parent study who also then participated in the QoL study were asked to participate in the present investigation. Contact information (i.e., phone number, address) of participants was updated by contacting patients over the telephone, and looking up information on the internet. Participants were contacted by this researcher over the telephone to discuss the project and to determine participants’ willingness to participate in the study. Participants were asked to fill out questionnaires that were delivered through the mail to obtain data on PD and QoL since the original study was concluded.

Questionnaires

Questionnaires for this follow-up study were essentially the same as the questionnaires sent in the original study (McRae et al., 2004) and were sent through the mail to participants. The questionnaires included instruments that assessed QoL while living with PD. Of the 30 participants from the original study, updated contact information was identified for 14 people. These 14 participants were asked to complete the questionnaire, and return it in the postage-paid envelope. Of the 14 questionnaires sent out, only 11 were returned. Follow-up phone calls were made to the remaining participants to determine if there were any problems, and to encourage them to return the questionnaires.

Data gathered from the received questionnaires were then compared to baseline, one-year, and two-year information that was previously collected from the participants. Trajectories regarding change over time were also determined.
Measures

The following measures can be found in Appendices A through L. These measures were sent to participants in the mail to be filled out and returned to the investigator. QoL measures were divided into three categories: Physical functioning, Emotional functioning, and Social functioning.

Physical Functioning

Participants’ level of Physical functioning related to PD was assessed by using the patient version of the Unified Parkinson’s Disease Rating Scale (UPDRS). The scale was developed by Montgomery et al. in 1994 and is an adaptation of the original scale (Fahn & Elton, 1987), which is used mainly by medical personnel to assess physical abilities and problems. Montgomery et al. (1994) established reliability estimates of the patient version of the UPDRS through its use in a health promotion program. The authors found that reliability for each of the scales ranged from .65 to .90. The UPDRS has been found to have satisfactory construct validity assessed across other instruments measuring PD (Ramaker, Marinus, Stiggelbout, & Johannes van Hilten, 2002). The UPDRS was utilized to measure the patients’ perspective of Physical functioning abilities and problems related to PD. Four scales were used: Activities of Daily Living (ADLs) at “Best” and “Worst” and Severity of Symptoms at “Best” and “Worst.” The scales ADLs at Best (when patients are physically “at their best”) and ADLs at Worst (when patients are physically “at their worst”), each include eight items with ranging scores from (1) Normal, (2) Adequate, (3) Limited, (4) Need Help, to (5) Unable to Do. Each scale was separately scored, with scores ranging from 8 to 40 points, with lower scores indicating better
functioning. A sample item from the ADL Scale is, “How well can you turn in bed at your best?” Participants were asked to rate their ability to turn in bed ranging from (1) Normal, (2) Adequate, (3) Limited, (4) Need Help, and (5) Unable to Do.

The Severity of Symptoms Scale includes five problems, which participants score at “Best” and “Worst” functioning. Each item is rated on the following scale: (1) Normal, (2) Mild, (3) Moderate, (4) Severe, and (5) Very Severe. The range of scores is from 5 to 25, with lower scores indicating better functioning. A sample item from the Severity of Symptoms Scale is, “Please rate the severity of tremor at your worst.” Participants were asked to rate the severity of tremor on a scale ranging from 1 (Normal) to 5 (Very Severe).

The Free or Restricted Scale was also used to assess Physical functioning of QoL. This single, global item measured how free or restricted the person felt “in doing what you want to do.” A Likert scale ranging from 1 (I still do everything I want to do) to 7 (I can no longer do the things I want to do) was used. Lower scores indicate better outcomes.

Emotional Functioning

The Parkinson’s Disease (PD) Stress Scale was developed to administer to German patients with PD (Ellgring, Macht, & Schwartz, 1993, unpublished data). This scale has 19 items, with lower scores indicating less stress. Patients were asked to indicate either “yes” or “no” as to whether each item described caused them considerable stress, or clearly bothered them. Sample items include, “sometimes I am embarrassed in public because of my symptoms,” and “I am anxious about the uncertainty of the future.
of my disease.” The estimate of reliability (Cronbach’s alpha) for the scale was .77 (McRae et al., 2004). The Parkinson’s Disease Stress Scale was based on Ellgring’s unpublished work. At the time of its initial inclusion in the study, the scale had not yet been validated. It was used in this study without other supporting information, such as a measure of validity.

The Center for Epidemiologic Studies Depression Scale (CESD; Radloff, 1977) was used to assess depressive affect related to QoL. The scale is comprised of 20 items and is a self-report assessment of the number and frequency of symptoms of depression. Each item is rated on a 4-point scale ranging from 0 to 3 related to frequency of experiencing depressive symptoms. Lower scores indicate less depression. For example, 0 indicates “less than 1 day” and 3 indicates “5 to 7 days.” Sample items include, “I was bothered by things that usually don’t bother me” and “I had trouble keeping my mind on what I was doing.” Possible total scores could range from 0 to 60.

Based on the original study, internal consistency for the CESD was found to be .89 (Radloff, 1977). Test-retest reliability was found to be acceptable. Radloff also reported the CESD as having excellent concurrent validity by clinical and self-report criteria, and substantial evidence of construct validity. The measure was found to be highly related to other depression measures that utilize self-report (Radloff, 1977). Craig, Richardson, Pass, and Bregman (1985) found a convergent validity measure of 0.65 when comparing the CESD with the Hamilton Rating Scale for Depression, an established assessment for depression. According to Hughes et al. (1993), CESD scale items have been shown to have satisfactory internal consistency, acceptable test-retest stability, good concurrent validity, and adequate construct validity.
The State-Trait Anxiety Inventory-State (STAI-State; Spielberger, Gorsuch, & Lushene, 1970) was developed to assess current, situational aspects of anxiety. State anxiety refers to the temporary condition of a person, based on changes in the environment, while trait anxiety refers to stable individual differences in anxiety. Environmental changes that have little effect on trait anxiety appear to have a more significant influence on state anxiety (Metzger, 1976). On this assessment, 20 items are rated on a 4-point scale ranging from 1 (not at all) to 4 (very much). Lower scores indicated less anxiety. Some examples of questions on this measure include “I feel calm” and “I feel jittery.”

An early published reliability estimate for the State-Trait Anxiety Inventory-State was .89 (Finch Jr., Montgomery, & Deardorff, 1973). Metzger (1976) found the assessment to have good discriminating ability for both high and low scoring participants. The STAI-State form has been assessed to be a valid measure of anxiety. Okun, Stein, Bauman, and Silver (1996) concluded that the STAI-State was a valid measure to assess anxiety due to supported content validity. The authors established good content validity by comparing the STAI-State to the DSM-IV criteria for Generalized Anxiety Disorder (Okun, Stein, Bauman, & Silver, 1996).

The Intrusiveness of Illness Scale is a 15-item scale that measured the degree to which a chronic illness interferes with usual life activities (Devins et al., 1984). This self-report questionnaire measures the extent to which the chronic illness, in addition to the treatment to the illness, hinders each of 15 life domains that are important to QoL (Devins, 1994). The range of responses for individual items was from 1 (very little) to 7 (a great deal). Lower scores indicated less intrusiveness. A total score on the
Intrusiveness of Illness Scale can range from 15 to 105 (Devins, 1994). Examples of items included, “How much does your illness interfere with your ability to work” and “How much does your illness interfere with your personal relationships with friends?”

The estimate of internal consistency reliability of the Intrusiveness of Illness Scale has been consistently high, ranging from .80 to .88 (Devins et al., 1984). When examined among participants who do not experience changes in their chronic illness or treatment, test-retest reliability has also been high. The Intrusiveness of Illness Scale has substantial face validity for participants who have a chronic illness, and can typically be completed in 10 minutes (Devins, 1994). Findings from groups of participants with different chronic illnesses support the construct validity of the instrument. For example, the level of illness intrusiveness for a sample of patients with multiple sclerosis was associated with increased physical disability, neurological impairment, and severity of the condition, which was indicated by the standard physical examination (Devins, 1994).

Social Functioning

The Social Provisions Scale (Cutrona & Russell, 1987) is a 24-item scale that measures the perceived degree to which participants' social relationships provide various dimensions of social support. The scale is intended to measure participants’ level of perceived social support. The instrument contains 4 items each for categories of social relationships, including guidance, reliable alliance, attachment, social integration, reassurance of worth, and opportunity to provide nurturance (Cutrona, 1987). A 4-point Likert scale ranging from 1 (strongly disagree) to 4 (strongly agree) is used. Lower scores indicated less perceived support. Total scores could range from 24 to 96. Examples of
items on this measure are “There is someone I could talk to about important decisions in my life” and “I have relationships where my competence and skills are recognized.”

The estimate of reliability for the Social Provisions Scale was reported to be .91 (Cutrona, 1989). Cutrona, Russell, and Rose’s (1984) study found internal consistency to be above .70 across all provisions when studying 100 elderly subjects. Test-retest reliability estimates were found to range from .37 to .66 (Cutrona, Russell, & Rose, 1984).

In a study of first-time mothers, Cutrona (1984) found the Social Provisions Scale dimensions of reliable alliance, reassurance of worth, social integration, and guidance demonstrated predictive validity of postpartum depression. Women without the six provisions of social relationships were more likely to become depressed after their pregnancy (Cutrona, 1984). Discriminant validity estimates across the six provisions range from .10 to .51 (Cutrona & Russell, 1987). Social integration, reassurance of worth, and guidance provisions were found to be significantly related to scores on the UCLA Loneliness Scale, demonstrating construct validity (Russell, Peplau, & Cutrona, 1980).

The Social Contact Scale was developed for the original QoL study by McRae et al. (2004). This measure assesses the amount of social interaction or activity experienced by the participant. The scale is intended to measure participants’ level of actual social support from others. Three items assessing the amount of socializing with friends, telephone communication, and participation in public activities were scored on a 6-point scale ranging from 1 (not at all) to 6 (all the time). Sample items included, “In the past month, how often did you get together socially with friends or relatives” and “During the past month, about how often have you done things in public such as shopping, eating in
restaurants, going to concerts or movies, etc.? As a follow-up to each of the three items, individuals were asked how satisfied they felt about this level of social contact. Level of satisfaction was rated on a Likert scale ranging from 1 (not at all happy) to 7 (extremely happy).

The estimate of reliability for the Social Contact Scale was .69 (McRae et al., 2004). Measures of social networks, such as social contact and number of relationships, were found to correlate with scores on the Social Provisions Scale (Cutrona & Russell, 1987). Progression of chronic illness appears to be correlated with loss of social contact (Ellgring, 1999; Lee et al., 1994; McNamara, Durso, & Harris, 2006). The Social Contact measure was developed for the original QoL study (McRae et al., 2004). It was used in this study to assess current level of actual social contact, and helped to determine the long-term effects of participants’ social QoL.

NEO Five-Factor Inventory

The NEO Five-Factor Inventory (NEO-FFI) is a 60 item measure of the Five Factor Model of personality, which includes Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness (Costa & McCrae, 1992). Items (descriptions of behavior) are answered on a five point Likert scale, ranging from “strongly disagree” to “strongly agree.” Sample items from the inventory include, “I often feel tense and jittery” and “I am seldom sad or depressed.” The NEO Five-Factor Inventory was administered as a separate assessment from the questionnaire.

McRae et al. (2003) investigated the effects of fetal transplantation surgery on personality for participants in the double-blind placebo-controlled trial described earlier.
The NEO-FFI was administered to participants at baseline, 12, and 24 months after receiving the surgery. Results indicated that for all participants, there were no changes on any of the five factor scales from baseline to one-year after the surgery. There was a significant change among the transplant group that included a decrease in Conscientiousness from baseline to 24 months. There were no changes for those who were in the placebo group who then received the transplant. The authors concluded that personality generally remained stable over the two-year period.

It has been reported that retest reliability for the five factors range from .86 to .90, and internal consistency ranges from .68 to .90 (Costa & McCrae, 1992). The NEO-FFI has demonstrated validity and utility in a number of different contexts. It is one of the most frequently used measures of the Five-Factor model, and has been translated into several languages (McCrae & Costa, 2004).

**Data Analyses**

Data analyses included two stages, preliminary and primary analysis. During the preliminary analysis, demographic information and descriptive statistics were analyzed. Composite variables were also created.

For the primary analyses, data were analyzed using repeated measures analysis of variance (ANOVA). Data collected in the present study were compared to data collected at baseline, and one and two years following transplantation in the QoL study (McRae et al., 2004).

The repeated measures design is a frequently used ANOVA design in which all subjects participate under all levels of the independent variable. It is also referred to as a
totally within subjects design. The design method is commonly used in longitudinal research. A repeated measures design is used when participants have all received the same intervention, or have some important characteristic in common. In this study, the individuals participated in the fetal tissue transplantation study (Freed et al., 2001) for the purpose of testing an experimental procedure to treat PD. In the repeated measures ANOVA, all participants were measured under all conditions. The primary variable used included the three dimensions of QoL: Physical functioning, Emotional functioning, and Social functioning.

A repeated measures ANOVA was used to determine changes in participants’ responses on the three dimensions. The first research question was: What is the trajectory of change in QoL over time for the baseline, one-year, two-year, and current long-term follow-up assessments? Analyses were performed separately on the three original domains of QoL: Physical functioning, Emotional functioning, and Social functioning. The second research question was: Was there any change in personality based on results of the NEO-FFI from baseline to the one-year, two-year, and current long-term follow-up assessments? Again, the repeated measures analyses were used to investigate any long-term changes among the five variables of the NEO-FFI: Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness.

Summary

Chapter Three described the methodology used in the present study. Descriptions of the participants, procedure, QoL measures, and data analyses were provided. Chapter Four presents the preliminary and primary results of the study.
Chapter Four

Results of the Study

Overview

This chapter presents the results of the statistical analyses associated with the current study. The results of the preliminary analyses are discussed, which are then followed by the results of the primary analyses utilized to address the research questions. All preliminary and primary statistical analyses were performed using the Statistical Package for the Social Sciences version 15.0 (SPSS 15.0). All statistical analyses used two-tailed tests of significance with an alpha level set at $p < .10$ due to the small sample size.

Participants originally represented two treatment groups. Those in the original transplant group ($n = 3$) received the fetal tissue transplantation surgery initially during the parent study (Freed et al., 2001). Those in the optional transplant group ($n = 8$) received a sham surgery, and later the fetal tissue transplantation procedure during the parent study (Freed et al., 2001). In the present study, statistical analyses compared the QoL of participants at the baseline, one-year, two-year, and current assessments. Because the two treatment groups had surgery at least one year apart, some adjustments were needed to equate the time periods for follow-up assessments. In other words, baseline data for those in the transplant group were collected approximately two to three months before transplantation. However, because of the one-year period of the double-blind
condition, for those who initially received the sham surgery, baseline data would have been collected approximately 18 months before transplantation. In order to equate the time periods involved in the analyses, the 12 month assessment was substituted as the baseline assessment for the initial sham group. By using this method of “shifting the data” to represent time since surgery instead of calendar time, the data from the two original groups were able to be combined and analyzed in terms of baseline, one and two years after surgery, and the current assessment. The following preliminary and primary analyses were based on the “shifted” variables that were created by combining both groups into one group.

Preliminary Analyses

This section of the chapter is organized in the following manner: a) participant response to questionnaires; b) missing data; c) participants’ demographic information; d) descriptive statistics related to the variables analyzed in the research hypotheses; e) reliability of variables analyzed in the research hypotheses; f) correlations of Physical and Emotional functioning variables, including the assumptions of normality, linearity, and homoscedasticity, and the treatment of outliers; and g) discussion on the creation of composite variables.

Participant Response of Questionnaires

Participants from the original QoL study were contacted to determine if they would be interested in being involved in the current study. Of the 30 participants in the original study, updated contact information was available for 14 people. Questionnaires were returned by 11 participants.
Data were collected from a total of 11 questionnaires that measured QoL. The questionnaires included the three dimensions of QoL: Physical functioning, Emotional functioning, and Social functioning. The Physical functioning dimension of QoL was assessed by using the patient version of the Unified Parkinson’s Disease Rating Scale (UPDRS), including the Activity of Daily Living, Severity of Symptoms, and the Free or Restricted scales. The Emotional functioning dimension of QoL was assessed by using the Center for Epidemiological Studies- Depression Scale (CESD), the Intrusiveness of Illness Scale, the State-Trait Anxiety Inventory-State Scale (STAI), and the Parkinson’s Disease Stress Scale. The Social functioning dimension of QoL was assessed by using the Social Provisions Scale and the Social Contact Scale. These 11 questionnaires were then compared to data collected previously at different time periods, including baseline (prior to surgery), one-year after surgery, and two-years after surgery. There was very little missing data in the questionnaires.

Missing Data

There was very little missing data in this study, primarily because of participant commitment to the project, and perhaps because participants were paid $25 for each completed questionnaire. Participants were not paid for the most recent set of returned questionnaires.

Demographic Information

A demographic questionnaire (Appendix J) was used to collect information on the participants’ demographic characteristics, which are presented in Table 1. As previously stated in Chapter Three, this study was based on participants with PD who received fetal
tissue transplantation surgery 10-12 years ago. Participants represented two treatment groups, based on the time they received the fetal tissue transplantation surgery. Those in the original transplant group (n = 3) received the fetal tissue transplantation procedure initially during the parent study (Freed et al., 2001). Those in the optional transplant group (n = 8) received a sham surgery, and later the fetal tissue transplantation procedure during the parent study (Freed et al., 2001). For the purpose of the present study, the demographic data is presented for the total sample of 11 individuals who participated in the current iteration of data collection.

An interesting find when looking at the demographic information of the participants (Table 1) is that a majority of them are currently employed or volunteering, despite the progressive nature of PD. Participants 6, 10, and 11 currently are employed, while Participants 1, 2, 3, 7, 8, and 9 are currently volunteering.

Descriptive Statistics

Descriptive analyses of the QoL measures included in the study were performed to determine if the responses were normally distributed and if the data showed sufficient variability (see Table 2). The descriptive analyses included the number of respondents, means, and standard deviations. Each QoL dimension included four time periods representing baseline (prior to surgery), one year after surgery, two years after surgery, and the current assessment.

Descriptive analyses of the NEO Five-Factor Inventory (NEO-FFI) scales (Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness) were included to determine if the responses were normally distributed
and if the data showed sufficient variability (see Table 3). The descriptive analyses included the number of respondents, means, and standard deviations. All five components of the NEO-FFI included four time periods representing baseline (prior to surgery), one year after surgery, two years after surgery, and the current assessment.
Table 2

Descriptive Statistics of QoL Variables for Baseline, One-Year, Two-Year, and Current Assessment

<table>
<thead>
<tr>
<th>QoL Variable (includes time of assessment)</th>
<th>N</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Functioning</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activities of Daily Living at Worst Scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11</td>
<td>27.36</td>
<td>6.67</td>
</tr>
<tr>
<td>One-Year</td>
<td>11</td>
<td>23.82</td>
<td>7.78</td>
</tr>
<tr>
<td>Two-Year</td>
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<td>20.67</td>
<td>7.21</td>
</tr>
<tr>
<td>Current</td>
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<td>26.27</td>
<td>6.94</td>
</tr>
<tr>
<td>Severity of Symptoms at Worst Scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11</td>
<td>12.09</td>
<td>2.67</td>
</tr>
<tr>
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<td>9.24</td>
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<td>5.91</td>
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<td>3.49</td>
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<td>6.91</td>
<td>3.18</td>
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<td>3.09</td>
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Table 2, continued

Descriptive Statistics of QoL Variables for Baseline, One-Year, Two-Year, and Current Assessment

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<thead>
<tr>
<th>QoL Variable (includes time of assessment)</th>
<th>N</th>
<th>Mean</th>
<th>S.D.</th>
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<tr>
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<tr>
<td>Social Provisions Scale</td>
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<tr>
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<td><strong>Social Contact Scale</strong></td>
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<td>One-Year</td>
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<td>13.82</td>
<td>3.54</td>
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<td>Two-Year</td>
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<td>3.77</td>
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</tr>
</tbody>
</table>
Table 3

Descriptive Statistics of NEO-FFI Variables for Baseline, One-Year, Two-Year, and Current Assessment

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<tr>
<th>NEO-FFI Variable (includes time of assessment)</th>
<th>N</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
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<td>Neuroticism - Baseline</td>
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<tr>
<td>Neuroticism - One-Year</td>
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<td>14.09</td>
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<td>7.63</td>
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<td>Openness to Experience - Baseline</td>
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<td>4.00</td>
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<td>Conscientiousness - One-Year</td>
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<td>6.36</td>
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<td>6.08</td>
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<td>Conscientiousness - Current</td>
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<td>28.22</td>
<td>4.02</td>
</tr>
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</table>
Reliability of Measures

Estimates of reliability (Cronbach’s alpha) of QoL measures for the current assessment were conducted as part of the preliminary analyses (see Table 4). Because the Free or Restricted variable of the UPDRS is a single item, no reliability coefficient was calculated. Although two scales had somewhat low reliability values (Severity of Symptoms at Worst Scale and Parkinson’s Disease Stress Scale), it was decided to include these scales in the analyses because they were used in previous work with these data.
Table 4

Reliability of QoL Measures for Current Assessment

<table>
<thead>
<tr>
<th>QoL Measure at Current Assessment</th>
<th>Cronbach’s Alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Functioning</strong></td>
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</tr>
<tr>
<td>Activities of Daily Living at Worst Scale</td>
<td>.88</td>
</tr>
<tr>
<td>Severity of Symptoms at Worst Scale</td>
<td>.68</td>
</tr>
<tr>
<td><strong>Emotional Functioning</strong></td>
<td></td>
</tr>
<tr>
<td>Center for Epidemiological Studies - Depression Scale</td>
<td>.84</td>
</tr>
<tr>
<td>Intrusiveness of Illness Scale</td>
<td>.94</td>
</tr>
<tr>
<td>State-Trait Anxiety Inventory - State Scale</td>
<td>.86</td>
</tr>
<tr>
<td>Parkinson’s Disease Stress Scale</td>
<td>.67</td>
</tr>
<tr>
<td><strong>Social Functioning</strong></td>
<td></td>
</tr>
<tr>
<td>Social Provisions Scale</td>
<td>.95</td>
</tr>
<tr>
<td>Social Contact Scale</td>
<td>.84</td>
</tr>
</tbody>
</table>
Correlations of Quality of Life Variables

Correlations of the measures comprising the Physical and Emotional dimensions of QoL were calculated to describe the strength and direction of the linear relationship between the variables. The Social Provisions Scale and Social Contact Scale were not strongly correlated from the beginning of data collection so the Social functioning measures continued to be analyzed separately in this study.

First, the Physical functioning dimension of QoL was analyzed. Preliminary analyses were performed to indicate that there was no violation of the assumptions of normality, linearity, and homoscedasticity for the variables for Activities of Daily Living at Worst Scale, Severity of Symptoms at Worst Scale, and Free or Restricted Scale. An examination of the data indicated that the responses were normally distributed and that there was sufficient variability within the sample. Scores on each variable appeared to be relatively normally distributed after viewing the histograms. After inspecting the boxplot for each variable, participant 8 was considered to be an outlier for the Activities of Daily Living at Worst Scale. In addition to being a very small sample size, because the values of the 5% trimmed mean and mean for the Activities of Daily Living at Worst Scale appear to be close, this data remained in the data set. Shapiro-Wilks statistics for test of normality revealed no violations of the assumption of normality for the three variables of Physical functioning. In addition, the normal probability plots indicated a normal distribution. Scatterplots for all three variables indicated there was not a violation for the linearity and homoscedasticity assumptions. By there being no violations to the assumptions of normality, linearity, and homoscedasticity, the data were considered to be independent of one another.
The relationships between the Activities of Daily Living at Worst Scale, Severity of Symptoms at Worst Scale, and Free or Restricted Scale were investigated using a Pearson correlation coefficient. Correlation coefficients are presented in Table 5. Results indicated strong, positive correlations among the measures, which justified putting them together to create the composite variable of Physical functioning.

Next, the Emotional functioning dimension of QoL was analyzed. Preliminary analyses were performed to determine whether there were any violations of the assumptions of normality, linearity, and homoscedasticity for the measures of Center for Epidemiological Studies - Depression Scale (CESD), the Intrusiveness of Illness Scale, the State-Trait Anxiety Inventory - State Scale (STAI), and the Parkinson’s Disease Stress Scale. Scores on each variable appeared to be relatively normally distributed after viewing the histograms. After inspecting the boxplot for each variable, participant 3 was considered to be an outlier for the CESD. In addition to being a very small sample size, because the values of the 5% trimmed mean and mean for the CESD appeared to be close, these data remained in the data set. The boxplot also indicated that participant 11 was considered to be an outlier for the Parkinson’s Disease Stress Scale. In addition to being a very small sample size, because the values of the 5% trimmed mean and mean for the CESD appear to be close, this case remained in the data set. Shapiro-Wilks statistics for test of normality revealed no violations of the assumption of normality for the four measures comprising Emotional functioning. In addition, the normal probability plots indicated a normal distribution. Scatterplots for all three variables indicated there was not a violation for the linearity and homoscedasticity assumptions. By there being no
violations to the assumptions of normality, linearity, and homoscedasticity, the data were considered to be independent of one another.

The relationships between the Center for Epidemiological Studies- Depression Scale, the Intrusiveness of Illness Scale, the State-Trait Anxiety Inventory - State Scale, and the Parkinson’s Disease Stress Scale were investigated using a Pearson correlation coefficient. Correlation coefficients are presented in Table 6. Results indicated that two of the correlations were not strong (.14 and .03). However, because these four measures had been combined to create the composite variable Emotional functioning in previous work with these data, it was decided to proceed to the next step of preliminary analyses, which was determining the reliability of the composite variables.
Table 5

Correlation Coefficients for Physical Functioning Variables (scales of Unified Parkinson’s Disease Rating Scale)

<table>
<thead>
<tr>
<th>QoL Physical Functioning Variable</th>
<th>Activities of Daily Living at Worst</th>
<th>Severity of Symptoms at Worst</th>
<th>Free or Restricted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Activities of Daily Living at Worst Scale</strong></td>
<td>Pearson Correlation: <strong>.76</strong>&lt;br&gt;Significance: <strong>.01</strong>&lt;br&gt;N: 11</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Severity of Symptoms at Worst Scale</strong></td>
<td>Pearson Correlation: <strong>.61</strong>&lt;br&gt;Significance: <strong>.05</strong>&lt;br&gt;N: 11</td>
<td><strong>.75</strong>&lt;br&gt;<strong>.01</strong>&lt;br&gt;11</td>
<td>11</td>
</tr>
<tr>
<td><strong>Free or Restricted Scale</strong></td>
<td>Pearson Correlation: <strong>.61</strong>&lt;br&gt;Significance: <strong>.05</strong>&lt;br&gt;N: 11</td>
<td><strong>.75</strong>&lt;br&gt;<strong>.01</strong>&lt;br&gt;11</td>
<td>11</td>
</tr>
</tbody>
</table>

*p < .05 level, two tailed. **p < .01 level, two tailed.*
Table 6
Correlation Coefficients for Emotional Functioning Variables

<table>
<thead>
<tr>
<th>QoL Emotional Functioning Variable</th>
<th>Center for Epidemiological Studies</th>
<th>Intrusiveness of Illness Scale</th>
<th>State-Trait Anxiety Inventory</th>
<th>Parkinson’s Disease Stress Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center for Epidemiological Studies - Depression Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusiveness of Illness Scale</td>
<td>.38</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td>.28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>10</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>State-Trait Anxiety Inventory - State</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>.56</td>
<td>.14</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td>.09</td>
<td>.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>10</td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Parkinson’s Disease Stress Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>.71*</td>
<td>.60</td>
<td>.03</td>
<td>1</td>
</tr>
<tr>
<td>Significance</td>
<td>.02</td>
<td>.07</td>
<td>.92</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>10</td>
<td>10</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

*p < .05 level, two tailed.
Composite Variables

Composite variables were created for Physical functioning and Emotional functioning to reduce the number of variables and improve the strength of the statistical analyses. Based on previous research with these variables and the correlation among each set of variables, standardized scores (or z-scores) were created for each of the measures so they could then be combined to create a total z-score representing the composite variable. Scores for each measure were standardized at each period based on the mean and standard deviation of the measure at baseline. Estimates of reliability (Cronbach’s alpha) were then calculated for the composite variable of Physical functioning and Emotional functioning. Reliability estimates were .88 and .74 respectively (see Table 7).

Social functioning was assessed by the two individual scales, Social Provisions Scale and Social Contact Scale due to low correlations between the measures. For the following primary analyses, the two composite variables and two social support measures were used.
Table 7

Reliability of QoL Measures for Current Assessment - Composite Variables

<table>
<thead>
<tr>
<th>QoL Measure at Current Assessment</th>
<th>Cronbach’s Alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Functioning - Composite Variable</td>
<td>.88</td>
</tr>
<tr>
<td><strong>UPDRS scales:</strong></td>
<td></td>
</tr>
<tr>
<td>Activities of Daily Living at Worst</td>
<td></td>
</tr>
<tr>
<td>Severity of Symptoms at Worst</td>
<td></td>
</tr>
<tr>
<td>Free or Restricted</td>
<td></td>
</tr>
<tr>
<td>Emotional Functioning - Composite Variable</td>
<td>.74</td>
</tr>
<tr>
<td><strong>Center for Epidemiological Studies - Depression Scale</strong></td>
<td></td>
</tr>
<tr>
<td>Intrusiveness of Illness Scale</td>
<td></td>
</tr>
<tr>
<td>State-Trait Anxiety Inventory - State</td>
<td></td>
</tr>
<tr>
<td>Parkinson’s Disease Stress Scale</td>
<td></td>
</tr>
</tbody>
</table>
Primary Analyses

The preceding section addressed demographic information and other preliminary analyses. The following section focuses on the analyses and results for the research questions of the study. The alpha level was set at $p < .10$ for all statistical analyses due to the small sample size. By using the .10 alpha level, there is an increased chance that a Type I error might have occurred, and a decreased chance that a Type II error might have occurred.

Research Question #1
What is the trajectory of change in QoL over time for the baseline, one-year, two-year, and current long-term follow-up assessment? Analyses were performed separately on the three original domains of QoL: Physical functioning, Emotional functioning, and Social functioning.

A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes over time. Scores were first compared on the QoL dimension of Physical functioning at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery). The Physical functioning dimension of QoL included the following measures: Unified Parkinson’s Disease Rating Scale (UPDRS) scales of Activities of Daily Living at Worst and Severity of Symptoms at Worst, and the Free or Restricted variable.

Results of this analysis revealed a significant quadratic change in Physical functioning over time when comparing the baseline, one-year, two-year, and current
assessments, F (3,6) = 9.14, p < .05. The .53 multivariate partial eta squared indicated a large effect size (Keppell & Wickens, 2004). A profile plot is presented in Figure 1, which shows the mean values of Physical functioning for the baseline, one-year, two-year, and current assessments. It appears that marked improvement in Physical functioning occurred between baseline and two years following surgery with a decline in self-reported functioning occurring from two years to the current assessment.

Figure 2 demonstrates the line of progression of Physical functioning for each participant for the baseline, one-year, two-year, and current assessments. Physical functioning scores appear to have some minor fluctuation between the baseline and two-year assessments, while there was a considerable decline in scores between the two-year and current assessments.
Figure 1

Trajectory of Change of Physical Functioning for Baseline, One-Year, Two-Year, and Current Assessments (lower scores mean improved functioning)
Figure 2

Line of Progression of Physical Functioning for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (lower scores mean improved functioning)
A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes on the QoL dimension of Emotional functioning at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery). The Emotional functioning dimension of QoL included the following measures: Center for Epidemiological Studies - Depression Scale (CESD), the Intrusiveness of Illness Scale, the State-Trait Anxiety Inventory - State scale (STAI), and the Parkinson’s Disease Stress Scale.

Results of this analysis revealed a significant quadratic change in Emotional functioning over time when comparing the baseline, one-year, two-year, and current assessments, $F (3,5) = 5.15, p < .10$. The .42 multivariate partial eta squared indicated a large effect size (Keppell & Wickens, 2004). A profile plot is presented (see Figure 3) to show the mean values of Emotional functioning for the baseline, one-year, two-year, and current assessments. In a profile very similar to Physical functioning, there appears to be an improvement in Emotional functioning that occurred between baseline and two years following surgery with a decline in Emotional functioning occurring from two years to the current assessment.

Figure 4 demonstrates the line of progression of Emotional functioning for each participant for the baseline, one-year, two-year, and current assessments. Emotional functioning scores appear to have some minor fluctuation between the baseline and two-year assessments, while there was a more significant decline in scores between the two-year and current assessments.
Figure 3

Trajectory of Change of Emotional Functioning for Baseline, One-Year, Two-Year, and Current Assessments (lower scores mean improved functioning)
Figure 4
Line of Progression of Emotional Functioning for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (lower scores mean improved functioning)
A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes on the QoL dimension of Social functioning at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery). The Social functioning dimension of QoL that was examined in this analysis was the Social Provisions Scale.

There was a significant cubic effect for time, $F(3,6) = 7.85, p < .05$ for the Social Provisions Scale. The .50 multivariate partial eta squared indicated a large effect size (Keppell & Wickens, 2004). Between the two-year assessment and the current assessment, perceived social support dropped well below previous levels. A profile plot is provided (see Figure 5) to indicate the mean values of Social functioning from the Social Provisions Scale for the baseline, one-year, two-year, and current assessments.

Figure 6 demonstrates the line of progression of Social functioning from the Social Provisions Scale for each participant for the baseline, one-year, two-year, and current assessments. Based on the figure, scores dropped between the baseline and two-year assessments. Scores greatly decreased between the two-year and current assessments.
Figure 5

Trajectory of Change of Social Provisions Scale for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Figure 6

Line of Progression of Social Functioning from the Social Provisions Scale for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes on the QoL dimension of Social functioning at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery). The Social functioning dimension of QoL that was examined in this analysis was the Social Contact Scale.

Results of this analysis revealed there were no significant changes in Social functioning over time when comparing the Social Contact Scale from the baseline, one-year, two-year, and current assessments. A profile plot is presented (see Figure 7) to show the mean values of Social functioning from the Social Contact Scale for the baseline, one-year, two-year, and current assessments.

Figure 8 demonstrates the line of progression of Social functioning from the Social Contact Scale for each participant for the baseline, one-year, two-year, and current assessments. Participants’ scores remained relatively consistent between the baseline and two-year assessments, while there was a steady drop in scores between the two-year and current assessments.
Figure 7

Trajectory of Change of Social Contact Scale for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Figure 8

Line of Progression of Social Functioning from the Social Contact Scale for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Research Question #2

Was there any change in personality based on results of the NEO-FFI for the baseline, one-year, two-year, and current long-term follow-up assessment? Analyses were performed separately on the five variables of the NEO-FFI: Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness.

A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes over time. Scores were first compared on the NEO-FFI variable of Neuroticism at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery).

Results of this analysis revealed there was a significant cubic change in Neuroticism over time when comparing the baseline, one-year, two-year, and current assessments, $F(3,5) = 4.55, p < .10$. The .39 multivariate partial eta squared indicated a large effect size (Keppell & Wickens, 2004). A profile plot shown in Figure 9 presents the mean values of Neuroticism for the baseline, one-year, two-year, and current assessments. This figure indicates that Neuroticism increased a great deal between the two-year and current assessments.

Figure 10 demonstrates the line of progression of Neuroticism for each participant for the baseline, one-year, two-year, and current assessments. This figure indicates that while there was a decline in scores between the one-year and two-year assessments, scores across participants increased between the two-year and current assessments.
Figure 9

Trajectory of Change of NEO-FFI: Neuroticism for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Figure 10

Line of Progression of Neuroticism from the NEO-FFI for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes of the NEO-FFI variable of Extraversion at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery).

There was a significant effect for time (cubic pattern of change) for the Extraversion variable of the NEO-FFI, $F(3, 5) = 6.95, p < .05$. The .50 multivariate partial eta squared indicated a large effect size (Keppell & Wickens, 2004). A profile plot is presented (see Figure 11) which indicates the mean values of Extraversion for the baseline, one-year, two-year, and current assessments. Scores decreased after baseline, and improved between the one-year and two-year assessments. Scores decreased between the two-year and current assessments.

Figure 12 demonstrates the line of progression of Extraversion for each participant for the baseline, one-year, two-year, and current assessments. This figure also indicates a fluctuation between scores over the four time periods.
Figure 11

Trajectory of Change of NEO-FFI: Extraversion for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Figure 12
Line of Progression of Extraversion from the NEO-FFI for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)

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Missing Data
A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes of the NEO-FFI variable of Openness to Experience at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery).

There was a significant effect for time (cubic pattern of change) for the Openness to Experience variable of the NEO-FFI, $F(3, 5) = 8.66, p < .05$. The .55 multivariate partial eta squared indicated a large effect size (Keppell & Wickens, 2004). The greatest amount of change occurred between the two-year and current assessments. A profile plot is presented (see Figure 13) to indicate the mean values of Openness to Experience for the baseline, one-year, two-year, and current assessments. According to Figure 13, scores decreased after baseline, but improved between the one-year and two-year assessments. Based on the figure, scores appear to have decreased significantly between the two-year and current assessments.

Figure 14 demonstrates the line of progression of Openness to Experience for each participant for the baseline, one-year, two-year, and current assessments. According to Figure 14, scores improved between the baseline and two-year assessments, but then dropped over time.
Figure 13

Trajectory of Change of NEO-FFI: Openness to Experience for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Figure 14

Line of Progression of Openness to Experience from the NEO-FFI for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes of the NEO-FFI variable of Agreeableness at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery).

Results of this analysis revealed there were no significant changes in Agreeableness over time when comparing the baseline, one-year, two-year, and current assessments. A profile plot is presented (see Figure 15) to show the mean values of Agreeableness for the four time periods.

Figure 16 demonstrates the line of progression of Agreeableness for each participant for the baseline, one-year, two-year, and current assessments. Scores appeared to fluctuate between the baseline and two-year assessments.
Figure 15

Trajectory of Change of NEO-FFI: Agreeableness for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Figure 16
Line of Progression of Agreeableness from the NEO-FFI for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)

**Missing Data**
A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes of the NEO-FFI variable of Conscientiousness at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery).

There was a significant cubic effect for time for Conscientiousness when comparing the baseline, one-year, two-year, and current assessments, $F (3,5) = 4.8, p < .10$. The .41 multivariate partial eta squared indicated a large effect size (Keppell & Wickens, 2004). A profile plot is shown (see Figure 17) to present the mean values of Conscientiousness for the baseline, one-year, two-year, and current assessments. There appears to be a progressively downward trend in the data over time, especially from the two-year assessment to the present.

Figure 18 demonstrates the line of progression of Conscientiousness for each participant for the baseline, one-year, two-year, and current assessments. According to the figure, scores decreased after the baseline assessment, then improved slightly until the two-year assessment. Scores generally declined between the two-year and current assessments.
Figure 17

Trajectory of Change of NEO-FFI: Conscientiousness for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
Figure 18

Line of Progression of Conscientiousness from the NEO-FFI for Each Participant for Baseline, One-Year, Two-Year, and Current Assessments (higher scores mean improved functioning)
There were 30 participants in the original QoL study (McRae, 2004). Of that number, some participants in the original sham surgery group did not receive the transplant, some participants passed away, while others were either not able to be located due to outdated contact information or were not interested in participating in the current study. Therefore, there were only 11 participants in the present investigation.

In order to examine differences between the 11 current participants and the other 19 participants in the original QoL study, scores on QoL, medical, and personality variables were compared. Results indicated that participants’ age ($p < .01$), gender ($p < .10$), level of actual support ($p < .05$), Extraversion ($p < .10$), and Openness to Experience ($p < .05$) were found to be significantly different when comparing participants in the present study to the remaining participants from the QoL study. Participants were younger in the present investigation when compared to the remaining QoL participants. There were also more female participants in the current study. Participants in the present investigation also reported higher levels of actual support, Extraversion, and Openness to Experience.

There were no significant differences between the means of the participants in the present study and the remaining participants from the original QoL study for the Physical and Emotional functioning dimensions of QoL, medical variables, or for the personality factors of Neuroticism, Agreeableness, and Conscientiousness.

**Summary**

Chapter Four presented the results of the statistical analyses associated with the current study. The results of the preliminary analyses were discussed, which were
then followed by the results of the primary analyses utilized to address the research questions.

A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes over time with an alpha level set at \( p < .10 \). Scores were compared on the QoL dimensions of Physical functioning, Emotional functioning, and Social functioning at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery). Results of the analyses revealed there was a significant effect for time for the Physical functioning, Emotional functioning, and Social Provisions Scale variables of QoL.

A one-way repeated measures analysis of variance (ANOVA) was conducted to assess longitudinal changes over time with an alpha level set at \( p < .10 \) on the five variables of the NEO-FFI: Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness. Results of the analyses revealed there was a significant effect for time for the Neuroticism, Extraversion, Openness to Experience, and Conscientiousness scales of the NEO-FFI. All effect sizes for significant changes were considered to be large. This indicated a very large magnitude of change, suggesting there was a strong effect between the fetal tissue transplantation surgery and the QoL variables and NEO-FFI factors.

Chapter Five will discuss the results presented in Chapter Four, as well as the limitations associated with this study and recommendations for future research.
Chapter Five

Discussion

Overview

Chapter Five will cover the following topics: a) brief summary of the study, b) discussion of the overall findings related to the research questions, c) limitations of the study, d) recommendations for future research, and e) conclusions.

Summary of the Study

Research has led to great improvements in surgical techniques for PD. Surgical procedures for PD may be considered when drug therapy is no longer effective. Different surgical procedures have been used over time to reduce symptoms of the disease. Since 1988, patients with PD have been involved in clinical trials investigating the efficacy of neural transplantation of fetal tissue into the brains of those affected with the disorder (Clarkson & Freed, 1999). Fetal tissue transplantation surgery has been used as an experimental surgical treatment to improve PD symptoms (Bethchen & Kaplitt, 2003; Freed, Greene, & Breeze, 2001).

While there is little research on the effectiveness of fetal tissue transplantation surgery as a treatment for PD, there is even less literature on long-term effects of this treatment (Hagell et al., 2002; Rosser & Dunnett, 2003). An even more limited amount of research exists on how QoL is affected by fetal tissue transplant surgery (McRae et al., 2004) in those with PD.
This study examined the longitudinal effects on QoL for individuals who participated in a fetal tissue transplantation surgery trial beginning in 1995. Participants were part of a parent study (Freed et al., 2001) that determined the effectiveness of fetal tissue transplantation. In the parent study (Freed et al., 2001), 20 participants were randomly assigned to receive the fetal tissue transplantation procedure, while the other 20 participants received a sham surgery with the understanding that they could receive the fetal tissue transplantation procedure at a later time. Patients and medical staff were blind to the type of surgery participants received until 13 months following the surgery. The purpose of the parent study was to assess whether participants who received the fetal tissue transplantation procedure improved significantly more than those who received the sham surgery, or placebo.

Participants were asked to complete questionnaires assessing QoL (McRae et al., 2004). Data were collected before surgery, and at four, eight, and 12 months after surgery before the blind was lifted. The purpose of the original QoL study was to determine if there were differences in QoL when comparing those who received the fetal tissue transplantation procedure to those who received the sham surgery (McRae et al., 2004).

In the present study, current data collected on QoL were compared with baseline, one-year, and two-year data on QoL from the original study (McRae et al., 2004). The study specifically addressed the following research questions:

1. What was the trajectory of change in QoL over time for the baseline, one-year, two-year, and current long-term follow-up assessment? Analyses were performed
separately on the three original domains of QoL: Physical functioning, Emotional functioning, and Social functioning.

2. Was there any change in personality based on results of the NEO-FFI for the baseline, one-year, two-year, and current long-term follow-up assessment?

Discussion of Overall Findings

The first research question was investigated to determine longitudinal changes of the three dimensions of QoL for those who received the fetal tissue transplantation surgery. Scores were first compared on the QoL dimension of Physical functioning at the following times that assessments were administered: baseline (prior to receiving fetal tissue transplantation), one year after the surgery, two years after the surgery, and the current assessment (10-12 years after the surgery) to assess longitudinal changes over time. The Physical functioning dimension of QoL included the following measures: Unified Parkinson’s Disease Rating Scale (UPDRS) scales of Activities of Daily Living at Worst and Severity of Symptoms at Worst, and the Free or Restricted variable.

Results of this analysis revealed a significant quadratic change in Physical functioning over time when comparing the baseline, one-year, two-year, and current assessments. Patients reported an improved level of Physical functioning from baseline to the two years following surgery (lower scores mean better functioning). Most improvement was reported between the baseline and one-year assessments (about .4) with improvement from one year to two years being half that, or about .2. In the interval between the two-year and the current assessments (an average of nine years), most patients reported a decline in Physical functioning. Patients reported having reduced
Physical functioning after the two-year assessment up to the present time. Impairment in Physical functioning might include more difficulty with performing activities of daily living, such as walking, writing, and talking. Greater impairment in Physical functioning could also include an increase in participants’ severity of symptoms, such as more severe tremors, greater difficulty with swallowing, or a higher frequency of falls. Participants may also currently feel that they cannot do the things they want to do, when compared to assessments at previous time periods. This trend in a decline in Physical functioning might be expected due to PD’s chronic, progressive nature (Guttman, Kish, & Furukawa, 2003; Hagell et al., 2002). It is interesting to note that in Figure 2, one person (Participant 2) reported improvement in Physical functioning from the two-year to the current assessment. Because of the varying amounts of time between the two-year and current assessments and because there were no intermediate assessments made after two years, it is impossible to determine a more exact trajectory of change over time.

Results of the current study revealed a significant quadratic change in Emotional functioning across time. Participants reported improved Emotional functioning between the baseline and two-year time period. Consistent with Physical functioning, there was a decrease in Emotional functioning between the two-year and current assessments (lower scores mean better functioning). In addition to an improvement in Physical functioning, Figure 4 indicates that Participant 2 reported improvement in Emotional functioning from the two-year to the current assessment. Participant 4 also improved in Emotional functioning from the two-year to the current assessment. As in Physical functioning, it is impossible to determine a more exact trajectory of change over time due to the varying amounts of time between the two-year and current assessments and because there were
no intermediate assessments made after two years. A decrease in Emotional functioning indicated a higher level of stress, depression, anxiety, and degree to which the PD interferes with participants’ usual life activities. Depression, stress, and anxiety may also be influenced by changes in lifestyle, relationships, drug treatment, and unrealistic expectations for the outcome (Leader & Leader, 2001) of the fetal tissue transplantation surgery.

Trajectory of change of the Social functioning dimension of QoL was also assessed. There was a significant cubic effect in participants’ level of perceived social support that was measured by the Social Provisions Scale (Cutrona & Russell, 1987). All three scores were within 1 standard deviation of the normative score of 82 (SD = 10; Cutrona & Russell, 1987). Participants’ scores indicated that Social functioning decreased between the baseline and two-year assessments. Level of perceived social support was greatly reduced between the two-year and current assessments from an average score of 83.33 to 72.89. This is quite an unusual result as perceived support does not typically change so dramatically over time (D. Russell, personal communication, June 12, 2009). Figure 6 shows that of the nine participants reporting data on the current assessment, only three maintained or improved their scores in terms of perceived support. Given that the Physical and Emotional dimensions of QoL appeared to worsen over time, it is understandable that this could negatively impact participants’ level of perceived support from others, intimacy and relationships with others, and feeling recognized and respected by others (Cutrona & Russell, 1987).

While perceived level of social support was significantly different in the current assessment, actual level of social support, as measured by the Social Contact Scale, was
not found to change significantly over time. Inspection of Figure 7, which shows the trajectory of change, indicates that participants appeared to have experienced a decline in actual support from others. Specifically, participants reported a decreased frequency in socializing with friends, telephone communication, and participation in public activities (McRae et al., 2004). These results are consistent with the decrease over time in participants’ level of perceived support. However, no causal relationships between the two types of social support can be established. It may be that a decline in Physical functioning impacted the frequency of being able to interact with others, which then led to a decrease in perceived social support. Even though there was a steady decline in the frequency of social interactions and activities with others, there was not found to be a statistically significant change over the four time periods that assessments were administered.

The second research question was to determine the trajectory of change for the five scales of the NEO-FFI for participants who participated in this study. According to existing research, the five factors of personality play an important role in producing individual differences in life satisfaction and other variables of well-being (Stephan, 2009). The five-factors of the NEO-FFI have been shown to be relatively stable over time. These factors are considered to represent traits of personality that are persistent through adulthood (Costa, Metter, & McCrae, 1994; Sørlie & Sexton, 2004).

Results of this analysis revealed significant differences among the participants for changes in Neuroticism, Extraversion, Openness to Experience, and Conscientiousness when comparing the baseline, one-year, two-year, and current assessments. Agreeableness did not change significantly over the four time periods. By looking at the
trajectory of change across the five factors, patients generally had a decrease in scores between the baseline and one-year assessments, and then an increase in scores between the one-year and two-year assessments. Finally, there was another decrease in scores between the two-year and current assessments. This pattern of change was found for the Extraversion, Openness to Experience, and Conscientiousness factors. In contrast, Neuroticism scores increased between the baseline and one-year assessments, and decreased between the one-year and two-year assessments. Neuroticism increased again between the two-year and current assessments.

Results of the analysis of Neuroticism indicated there was a significant cubic change in Neuroticism over the baseline, one-year, two-year, and current assessments. Levels in Neuroticism increased until one year after surgery. Between one and two years after surgery, levels in Neuroticism decreased back down to a level similar to baseline. Scores across participants increased between the two-year and current assessments. The level of Neuroticism in the current study exceeded any other levels from prior assessments.

Participants’ scores were at a mean of 14.88 at the baseline assessment, and then increased by two points at the one-year assessment. Levels of Neuroticism then decreased to 15 at the two-year assessment. Scores then increased to 19.25 with a regression to the mean (19.07) occurring between the two-year and current assessments (Costa & McCrae, 1992). Figure 10 indicates that of the 10 participants who completed the current assessment, six of them had an increase in Neuroticism between the two-year and current assessments. Neuroticism was not found to be a stable variable of personality, as
evidenced by the significant cubic change over time. Mroczek and Spiro (2005) found that high levels of Neuroticism were related to low life satisfaction.

There was also a significant cubic change in Extraversion across time. Participants appeared to feel less extraverted between the baseline and one-year assessments. Conversely, participants’ level of Extraversion increased between the one-year and two-year assessments, though not as high as Extraversion was found to be at baseline. Finally, Extraversion decreased again between the two-year and current assessments, this time to the lowest level across the four time periods.

Participants’ scores were at a mean of 30.88 at the baseline assessment, and then decreased by three points at the one-year assessment. Levels of Extraversion then increased to 29.88 at the two-year assessment. Scores then decreased to 26.88 with a regression to the mean (27.69) occurring between the two-year and current assessments (Costa & McCrae, 1992). Figure 12 indicates that of the 9 participants who completed the current assessment, five of them had a decrease in Extraversion between the two-year and current assessments. Extraversion was not assessed to be a stable variable of personality, as evidenced by the significant cubic change over time. Mroczek and Spiro (2005) also found that higher levels of Extraversion were related to greater life satisfaction.

A significant cubic change was also found for the factor Openness to Experience. Although levels of Openness to Experience decreased slightly between the baseline and one-year assessments (.5 points), and then increased between the one-year and two-year assessments (1.5 points), the factor appeared to remain relatively stable over the two year period. There was a more dramatic change in Openness to Experience between the two-year and current assessments (4 points).
Participants’ scores were at a mean of 34.63 at the baseline assessment, and then decreased by half a point at the one-year assessment. Levels of Openness to Experience then increased to 35.38 at the two-year assessment. Scores then decreased down to 31.38 with a regression to the mean (27.03) occurring between the two-year and current assessments (Costa & McCrae, 1992). Figure 14 indicates that of the 10 participants who completed the current assessment, seven of them had a decrease in Openness to Experience between the two-year and current assessments. Openness to Experience was not found to be a stable variable of personality, as evidenced by the significant cubic change over time.

There was a significant linear relationship for the Conscientiousness factor across time. Participants appeared to feel less Conscientiousness between the baseline and one-year assessments. Participants felt slightly more Conscientiousness between the one-year and two-year assessments, and then significantly less between the two-year and current assessments.

Participants’ scores were at a mean of 31.63 at the baseline assessment, and then decreased by two points at the one-year assessment. Levels of Conscientiousness then increased to 30.5 with a regression to the mean (34.57) occurring between the one-year and two-year assessments (Costa & McCrae, 1992). Scores then decreased to 27.75 between the two-year and current assessments. Figure 18 indicates that of the 9 participants who completed the current assessment, seven of them had a decrease in Conscientiousness between the two-year and current assessments. Similarly to the other factors of personality, Conscientiousness was not found to be a stable variable of personality, as evidenced by the significant linear change over time.
In the present study, Neuroticism, Extraversion, Openness to Experience, and Conscientiousness were not found to be stable variables of personality over time. There have been varying theories as to whether brain tissue transplantation alters personality (Northoff, 1996). McRae et al. (2003) found that personality basically remained stable during a two-year follow-up for participants who had received fetal tissue transplantation. Mendelsohn, Dakof, and Skaff (1994) found a negative change in personality in Parkinson’s disease patients and suggested that it was due to the duration of the disease rather than aging. Previous research on the NEO with people who have medical conditions such as cancer and coronary disease has suggested that a change in health status did not affect personality (Costa, Metter, & McCrae, 1994).

It is important to note that when looking at the individual scores of participants for the personality factors of the NEO-FFI, the majority of participants fell within one standard deviation of the normative scores for each factor. This indicates that the participants’ levels of personality were generally within “normal” limits. Overall, there does appear to be a regression to the mean effect for the personality variables. Although scores for some subscales (Extraversion, Open to Experience, and Agreeableness) initially were higher than normative scores, this may be explained in part by the nature of the experimental surgery and the types of individuals who were willing to participate in this type of procedure, where the collection of data attracted individuals who would be willing to take risks.

Participants reported more neuroticism, feeling less extraverted, less open to experiences, and less conscientiousness since the initial surgical procedure that occurred 10-12 years ago. This finding is consistent with participants’ decline in Physical
functioning, Emotional functioning, and perceived level of social support, as measured by the Social Provisions Scale (Cutrona & Russell, 1987). While some of these findings can perhaps be explained by progression of disease over time, other changes, as in the NEO-FFI scales, are more difficult to explain. Unfortunately, the design precludes investigation of causal relationships in this study.

Limitations of the Study

Several limitations exist in the present study. First, the sample size is small because the sample could only include the participants from the parent study (Freed et al., 2001), who then participated in the original study on QoL (McRae et al., 2004). Thus, the potential sample size was only 30. Of that number, some participants in the original sham surgery group did not receive the transplant, some participants passed away, while others were either not able to be located due to outdated contact information or were not interested in participating in the current study. Because of the experimental nature of the study and the small sample size, the significance level was allowed to be .10, increasing the chance that a Type I error might have occurred.

Results from this study cannot be generalized to other individuals with PD; hence, this study has poor external validity. The results of the study may not be applicable to all Parkinson’s patients due to the inclusion and exclusion criteria used to recruit participants in the parent study (Freed et al., 2001). Also, this was a very unique study that involved experimental surgery to determine the effects of fetal tissue transplantation surgery on motor symptoms as well as QoL. Aside from the limitations of the study, it provided a unique opportunity to investigate the longitudinal changes over time regarding QoL with
a specific population of individuals who participated in an experimental surgical procedure.

Results demonstrated a general pattern of improvement over the one or two year period after surgery, followed by a decline to the current assessment. What the pattern of improvement or decline may have looked like between two years post-surgery and the current assessment is impossible to predict without the data. However, we do know that the pattern of change was not the same for everyone, as demonstrated by the figures showing individual data. Further investigation to determine differences between those who improved and those who declined is warranted.

Recommendations for Future Research

Due to the small sample size, it is difficult to draw conclusions on fetal tissue transplantation surgery and QoL that are generalized to the greater population of those with PD. A recommendation for future studies is to assess the effects of treatment for PD with a larger sample size. The small sample size of this study resulted in limited external validity, low statistical power, and an increased risk of making a Type I error because of allowing the significance level to be .10. A larger sample would create an increase in statistical power, resulting in greater differentiation between the comparison of groups. However, because of the unique experimental nature of this study from the beginning, it is acknowledged that developing another study with a larger sample size will probably not happen.

Interestingly, participants’ level of perceived social support, as measured by the Social Provisions Scale, was found to significantly change over time, while participants’
level of actual support, as measured by the Social Contact Scale, was not found to change. Although there was a decrease in visits with friends, telephone contact, and activities in public, the change was not statistically significant over time. On the other hand, participants’ level of perceived social support was significantly reduced by the current assessment. It is not known why participants reported such a decline in perceived social support while their frequency in interactions with others was not found to be statistically significant. It is interesting for there to be such a difference between perceived and actual level of support, and this would be a fascinating topic for further investigation.

Further work is needed to identify exactly what contributed to changes in QoL and personality factors for participants in this study. It is important to determine, if possible, pre-surgical characteristics of those who improved versus those who declined over the period of the study. Further research is recommended to investigate QoL and changes in personality in older individuals in general, specifically when those individuals are managing a chronic illness. The results showing changes in four of the five scales of the NEO-FFI are clearly intriguing and suggest the need for further study.

Conclusions

The objective of the current study was to examine the changes in QoL for people who received fetal tissue transplantation for PD 10-12 years ago. This study is considered an important contribution to research on PD and QoL due to the unique nature of the sample and the longitudinal aspect of the study which incorporated assessments from four time periods.
The study found significant changes in several areas of QoL, including Physical functioning, Emotional functioning, and Social functioning, specifically the perceived level of social support. The study also found significant changes in the NEO-FFI personality factors of Neuroticism, Extraversion, Openness to Experience, and Conscientiousness over time. How these changes are related to one another and how and why some participants differed from others in terms of improvements and declines in functioning are questions for another study.
References


Appendix A

Letter Sent to Participants with Questionnaire

Dear

It has been several years since you participated in the fetal tissue transplant study for the treatment of Parkinson’s disease. We thank you for all the time you gave to fill out our questionnaires related to quality of life at that time. Because we are interested in the long-term effects of the surgery on patients and care partners/spouses, we would like to ask you to fill out an adapted version of previous questionnaires. I believe my assistant, Cindy Cole, has recently been in touch with you about your willingness to fill out this follow-up assessment.

Enclosed are the follow-up questionnaires related to patient and caregiver perspectives’ of Parkinson’s disease since the neural transplant surgery. There are two versions of the questionnaires. The patient version is green and reads “Patient Version” at the top of the front page. The caregiver version is yellow and reads “Caregiver Version” at the top of the front page. Once you have completed the questionnaires, please return them to us in the postage-paid envelope we have provided.

We really appreciate your participation in this project. Your responses are very important to us for better understanding your quality of life since the surgery. Once again, your identity will remain anonymous throughout the process of this study. We have enclosed one of the articles that explains some of the results of the earlier study. If you have any questions or concerns, please feel free to call me at (303) 871-2475 or email me at cmcrae@du.edu. Thank you again for your time and interest.

Very sincerely,

Cynthia McRae
University of Denver
Professor
Chair, Counseling Psychology Program
Appendix B

Unified Parkinson’s Disease Rating Scale (UPDRS) - Patient Version

How well can you perform these daily activities AT YOUR BEST?
(check one for each row)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Adequate</th>
<th>Limited</th>
<th>Need Help</th>
<th>Unable To Do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dressing</td>
<td></td>
<td></td>
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<tr>
<td>Cutting food</td>
<td></td>
<td></td>
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<tr>
<td>Hygiene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Getting up from chair</td>
<td></td>
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<td></td>
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<tr>
<td>Turning in bed</td>
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<tr>
<td>Writing</td>
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<tr>
<td>Talking</td>
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</tbody>
</table>

How well can you perform these daily activities AT YOUR WORST?
(check one for each row)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Adequate</th>
<th>Limited</th>
<th>Need Help</th>
<th>Unable To Do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking</td>
<td></td>
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<tr>
<td>Dressing</td>
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<tr>
<td>Cutting food</td>
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<tr>
<td>Hygiene</td>
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<tr>
<td>Getting up from chair</td>
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<tr>
<td>Turning in bed</td>
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<td>Writing</td>
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<tr>
<td>Talking</td>
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Appendix C

Severity of Symptoms

Please rate the severity of each of the following problems AT YOUR BEST. (check one for each row)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor</td>
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<tr>
<td>Swallowing</td>
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<tr>
<td>Salivation</td>
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<tr>
<td>Freezing when walking</td>
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<tr>
<td>Falling</td>
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</table>

Please rate the severity of each of the following problems AT YOUR WORST. (check one for each row)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
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</thead>
<tbody>
<tr>
<td>Tremor</td>
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<tr>
<td>Swallowing</td>
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<td>Salivation</td>
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<tr>
<td>Freezing when walking</td>
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<td>Falling</td>
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Appendix D

Free or Restricted Scale

Overall, how free or restricted do you feel in doing what you want to do? (check or circle the appropriate number)

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I still do everything I want to do</td>
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<tr>
<td></td>
<td>I can no longer do the things I want to do</td>
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Appendix E

Parkinson’s Disease Stress Scale

Below you will find a list of stressful situations that may occur because of your physical symptoms. Please check “Yes” or “No” to indicate whether or not an item causes you considerable stress, or clearly bothers you.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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<tbody>
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</table>

1. Sometimes I am embarrassed in public because of my symptoms.
2. I attract attention in public because of my symptoms.
3. Friends and acquaintances do not take my symptoms seriously.
4. I cannot make new friends because of my disease.
5. I am anxious about the uncertainty of the future of my disease.
6. I worry a great deal about my symptoms.
7. I worry so much about my disease that all other things become unimportant.
8. My physical condition tends to determine all that I think and do.
9. I feel like a disabled person.
10. I feel a sense of helplessness and anger because I cannot influence my disease.
11. The lives of my loved ones have changed because of my disease.
12. Even members of my family cannot really understand the difficulties I face.
13. My partner and my family take too little notice of my disease.
14. I am concerned that my family members restrict themselves too much because of my disease.
15. Sometimes I think my partner may leave me because of my disease.
Appendix E, continued

Parkinson’s Disease Stress Scale

Below you will find a list of stressful situations that may occur because of your physical symptoms. Please check “Yes” or “No” to indicate whether or not an item causes you considerable stress, or clearly bothers you.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
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<tbody>
<tr>
<td>___</td>
<td>___</td>
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</table>

16. Because of my disease I have had to give many personal responsibilities over to my partner or family members.

| ___ | ___ |

17. Because of my disease I have had to give up my job.

| ___ | ___ |

18. I have the impression that my disease is not being treated properly by my doctor.

| ___ | ___ |

19. I often cannot ask all my questions when I am with the doctor.
Appendix F

The Center for Epidemiologic Studies Scale (CESD)

Below is a list of ways you might have felt during the past week. Please indicate how often you felt or acted the way each statement suggests by using the following scale:

- Rarely or none of the time (Less than 1 day)
- Some or a little of the time (1-2 days)
- Occasionally or a moderate amount of time (3-4 days)
- Most all of the time (5-7 days)

<table>
<thead>
<tr>
<th>Statement</th>
<th>Rarely</th>
<th>Some of the Time</th>
<th>Moderate Amount of Time</th>
<th>Most of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I was bothered by things that usually don’t bother me.</td>
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<tr>
<td>2. I did not feel like eating; my appetite was poor.</td>
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<tr>
<td>3. I felt that I could not shake off the blues even with help from my family or friends.</td>
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<tr>
<td>4. I felt that I was just as good as other people.</td>
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<tr>
<td>5. I had trouble keeping my mind on what I was doing.</td>
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<tr>
<td>6. I felt depressed.</td>
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<tr>
<td>7. I felt that everything I did was an effort.</td>
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<tr>
<td>8. I felt hopeful about the future.</td>
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<tr>
<td>9. I thought my life had been a failure.</td>
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</tr>
<tr>
<td>10. I felt fearful.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. My sleep was restless.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix F, continued

The Center for Epidemiologic Studies Scale (CESD)

Below is a list of ways you might have felt during the past week. Please indicate how often you felt or acted the way each statement suggests by using the following scale:

Rarely or none of the time (Less than 1 day)
Some or a little of the time (1-2 days)
Occasionally or a moderate amount of time (3-4 days)
Most all of the time (5-7 days)

<table>
<thead>
<tr>
<th></th>
<th>Rarely</th>
<th>Some of the Time</th>
<th>Moderate Amount of Time</th>
<th>Most of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. I was happy.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>13. I talked less than usual.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>14. I felt lonely.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>15. People were unfriendly.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>16. I enjoyed life.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>17. I had crying spells.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>18. I felt sad.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>19. I felt that people disliked me.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>20. I could not get “going.”</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
</tbody>
</table>
Appendix G

State-Trait Anxiety Inventory-State

Listed below are a number of statements that people have used to describe themselves. Read each statement and then indicate how you feel at the present moment (check one answer for each item).

<table>
<thead>
<tr>
<th></th>
<th>Not At All</th>
<th>Somewhat</th>
<th>Moderately</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I feel calm.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. I feel secure.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. I am tense.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. I am regretful.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. I am at ease.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. I feel upset.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. I am worrying over possible misfortunes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. I feel rested.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. I feel anxious.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. I feel comfortable.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. I feel self-confident.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. I feel nervous.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. I am jittery.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. I feel “high-strung.”</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. I am relaxed.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix G, continued

State-Trait Anxiety Inventory-State

Listed below are a number of statements that people have used to describe themselves. Read each statement and then indicate how you feel at the present moment (check one answer for each item).

<table>
<thead>
<tr>
<th></th>
<th>Not At All</th>
<th>Somewhat</th>
<th>Moderately</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>16. I feel content.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. I am worried.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. I feel over-excited and “rattled.”</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. I feel joyful.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. I feel pleasant.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix H

Intrusiveness of Illness Scale

Using the scale below, check or circle the number that expresses how much you feel your Parkinson’s disease interferes with the following aspects of your life.

<table>
<thead>
<tr>
<th>My illness interferes with my…</th>
<th>Very Little</th>
<th>A Great Deal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Image</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Eating Habits</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Ability to Work</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Financial Security</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Preferred Recreation/Leisure</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Responsibility in the Family</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Family Relationships</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Marital Relationships</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Sexual Relationships</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Personal Relationships with Friends</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Plans for the Future</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Freedom to Choose Time Alone</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Ability to Express My Personality</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Sense of Independence</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>Self-Esteem</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
</tbody>
</table>
Appendix I

NEO Five-Factor Inventory (NEO-FFI)

Circle the response that best represents your opinion.

Circle SD if you strongly disagree or the statement is definitely false.
Circle D if you disagree or the statement is mostly false.
Circle N if you are neutral on the statement, if you cannot decide, or if the statement is about equally true and false.
Circle A if you agree or the statement is mostly true.
Circle SA if you strongly agree or the statement is definitely true.

1. I am not a worrier.  
2. I like to have a lot of people around me.  
3. I don’t like to waste my time daydreaming.  
4. I try to be courteous to everyone I meet.  
5. I keep my belongings neat and clean.  
6. I often feel inferior to others.  
7. I laugh easily.  
8. Once I find the right way to do something, I stick to it.  
9. I often get into arguments with my family and co-workers.  
10. I’m pretty good about pacing myself so as to get things done on time.  
11. When I’m under a great deal of stress, sometimes I feel like I’m going to pieces.  
12. I don’t consider myself especially “light-hearted.”
Appendix I, continued

NEO Five-Factor Inventory (NEO-FFI)

SD = Strongly Disagree  
D = Disagree  
N = Neutral  
A = Agree  
SA = Strongly Agree

13. I am intrigued by the patterns I find in art and nature.  
SD D N A SA

14. Some people think I’m selfish and egotistical.  
SD D N A SA

15. I am not a very methodical person.  
SD D N A SA

16. I rarely feel lonely or blue.  
SD D N A SA

17. I really enjoy talking to people.  
SD D N A SA

18. I believe letting students hear controversial speakers can only confuse and mislead them.  
SD D N A SA

19. I would rather cooperate with others than compete with them.  
SD D N A SA

20. I try to perform all the tasks assigned to me conscientiously.  
SD D N A SA

21. I often feel tense and jittery.  
SD D N A SA

22. I like to be where the action is.  
SD D N A SA

23. Poetry has little or no effect on me.  
SD D N A SA

24. I tend to be cynical and skeptical of others’ intentions.  
SD D N A SA

25. I have a clear set of goals and work toward them in an orderly fashion.  
SD D N A SA

26. Sometimes I feel completely worthless.  
SD D N A SA
Appendix I, continued

NEO Five-Factor Inventory (NEO-FFI)

SD = Strongly Disagree
D = Disagree
N = Neutral
A = Agree
SA = Strongly Agree

27. I usually prefer to do things alone. SD D N A SA
28. I often try new and foreign foods. SD D N A SA
29. I believe that most people will take advantage of you if you let them. SD D N A SA
30. I waste a lot of time before settling down to work. SD D N A SA
31. I rarely feel fearful or anxious. SD D N A SA
32. I often feel as if I’m bursting with energy. SD D N A SA
33. I seldom notice the moods or feelings that different environments produce. SD D N A SA
34. Most people I know like me. SD D N A SA
35. I work hard to accomplish my goals. SD D N A SA
36. I often get angry at the way people treat me. SD D N A SA
37. I am a cheerful, high-spirited person. SD D N A SA
38. I believe we should look to our religious authorities for decisions on moral issues. SD D N A SA
39. Some people think of me as cold and calculating SD D N A SA
### NEO Five-Factor Inventory (NEO-FFI)

SD = Strongly Disagree  
D = Disagree  
N = Neutral  
A = Agree  
SA = Strongly Agree

<table>
<thead>
<tr>
<th>Item</th>
<th>SD</th>
<th>D</th>
<th>N</th>
<th>A</th>
<th>SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>40.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>41.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>42.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>43.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>44.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>45.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>46.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>47.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>48.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>49.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>50.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>51.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

134
Appendix I, continued

NEO Five-Factor Inventory (NEO-FFI)

SD = Strongly Disagree
D = Disagree
N = Neutral
A = Agree
SA = Strongly Agree

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>52.</td>
<td>I am a very active person.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>53.</td>
<td>I have a lot of intellectual curiosity.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>54.</td>
<td>If I don't like people, I let them know it.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>55.</td>
<td>I never seem to be able to get organized.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>56.</td>
<td>At times I have been so ashamed I just wanted to hide.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>57.</td>
<td>I would rather go my own way than be a leader of others.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>58.</td>
<td>I often enjoy playing with theories or abstract ideas.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>59.</td>
<td>If necessary, I am willing to manipulate people to get what I want.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
<tr>
<td>60.</td>
<td>I strive for excellence in everything I do.</td>
<td>SD</td>
<td>D</td>
<td>N</td>
<td>A</td>
</tr>
</tbody>
</table>
Appendix J

Social Provisions Scale (SPS)

In answering the following questions, think about your current relationships with friends, family members, co-workers, community members, and so on. Please indicate to what extent each statement describes your current relationships with other people (check one answer for each item).

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. There are people I can depend on to help me if I really need it.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. I feel that I do not have close personal relationships with other people.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. There is no one I can turn to for guidance in times of stress.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. There are people who depend on me for help.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. There are people who enjoy the same social activities I do.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Other people do not view me as competent.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. I feel personally responsible for the well-being of another person.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. I feel part of a group who share my attitudes and beliefs.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. I do not think other people respect my skills and abilities.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. If something went wrong, no one would come to my rescue.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. I have close relationships that provide me with a sense of emotional security and well-being.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

136
Appendix J, continued

Social Provisions Scale (SPS)

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. There is someone I could talk to about important decisions in my life.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>13. I have relationships where my competence and skill are recognized.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>14. There is no one who shares my interests and concerns.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>15. There is no one who really relies on me for their well-being.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>16. There is a trustworthy person I could turn to for advice if I were having problems.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>17. I feel a strong emotional bond with at least one other person.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>18. There is no one I can depend on for aid if I really need it.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>19. There is no one I feel comfortable talking about problems with.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>20. There are people who admire my talents and abilities.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>21. I lack a feeling of intimacy with another person.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>22. There is no one who likes to do the things I do.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>23. There are people I can count on in an emergency.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>24. No one needs me to care for them.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
</tbody>
</table>
Appendix K

Social Contact Scale

During the past month, about how often did you get together socially with friends or relatives? (check one)

- [ ] Not at all
- [ ] About once a week
- [ ] Once in the past month
- [ ] Several days a week
- [ ] 2 or 3 times in the past month
- [ ] Every day

How happy are you with this level of contact?

1 2 3 4 5 6 7
Not at all happy Extremely happy

About how often were you on the telephone with close friends or relatives during the past month? (check one)

- [ ] Not at all
- [ ] About once a week
- [ ] Once in the past month
- [ ] Several days a week
- [ ] 2 or 3 times in the past month
- [ ] Every day

How happy are you with this level of contact?

1 2 3 4 5 6 7
Not at all happy Extremely happy

During the past month, about how often have you done things in public such as shopping, eating in restaurants, going to concerts or movies, etc.? (check one)

- [ ] Not at all
- [ ] About once a week
- [ ] Once in the past month
- [ ] Several days a week
- [ ] 2 or 3 times in the past month
- [ ] Every day

How happy are you with this level of contact?

1 2 3 4 5 6 7
Not at all happy Extremely happy
Appendix L

Participant Demographics

Information About You

1. What is your current living situation? (check one)
   - Living with a partner or family member
   - Living with a friend or roommate
   - Living alone
   - Living in a residential setting

2. What is your current marital status? (check one)
   - Never been married
   - Married or living with partner
   - Separated or divorced
   - Widowed

3. If you are married to your partner, how long have you been married? ____

4. If you are married, is this your: (check one)
   - first marriage
   - second marriage
   - third marriage

5. Do you have paid employment right now? (check one)
   - No
   - Yes, part-time
   - Yes, full-time

6. Do you currently do any volunteer work?
   - Yes
   - No
   - I used to, but no longer do
Appendix L, continued

Participant Demographics

7. If not currently employed, what is the main reason? (please check one box only)

____ Temporarily laid off
____ Retired by my own choice
____ Forced to retire by my employer
____ Retired on physician’s advice
____ Homemaker
____ Poor health
____ My job was too stressful, or physically demanding
____ Other reason (specify): ________________________________________

8. Do you have any other chronic health problems (e.g., diabetes, heart condition, high blood pressure)? (check one)

____ Yes If yes, please describe: _________________________________________
____ No