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A Longitudinal Study of Fetal Tissue Transplantation Surgery for the Treatment of Parkinson's Disease: Can Quality of Life and Optimism at Baseline Predict Patient Outcome 10 Years Later?

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A LONGITUDINAL STUDY OF FETAL TISSUE TRANSPLANTATION SURGERY FOR THE TREATMENT OF PARKINSON'S DISEASE: CAN QUALITY OF LIFE AND OPTIMISM AT BASELINE PREDICT PATIENT OUTCOME 10 YEARS LATER?

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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 for the treatment of advanced PD. The authors of that study examined 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 with 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 QoL among participants who received the fetal transplant surgery beginning in 1995. Participants included 11 people who were in the parent (Freed et al., 2001) and original QoL (McRae, 2004) studies. Participants completed several questionnaires that assessed many of the dimensions of QoL. Information from the questionnaires was compared to data collected before surgery, and at one and two years following surgery. Results indicated that Social functioning at baseline significantly predicted participants' Physical functioning over ten years later.

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Chapter One

Introduction

Description of Parkinson's Disease

Parkinson's disease (PD) is a chronic and progressive neurological disorder that severely impacts the quality of life of those who live with it. In 1817, the neurologist James Parkinson described a collection of symptoms that he called "Shaking Palsy." This initial description later became known as Parkinson's disease. Although knowledge of the pathology and clinical spectrum of PD has continued to evolve over time (Clarkson & Freed, 1999), the cardinal symptoms of the disease have remained the same. The primary physical symptoms of PD are characterized by tremor, muscle rigidity, bradykinesia (slowness of movement), akinesia (absence of movement), and difficulties with balance and walking (Bartels & Leenders, 2008). After several years these symptoms are typically not controlled well enough with medications or surgery to allow the patient to maintain a lifestyle they prefer (Behari, Srivastava, & Pandey, 2005).

Secondary non-motor symptoms of PD may include high levels of cognitive dysfunction, language difficulties, depression, and impaired functioning (Jankovic, 2008). Lezak (1983) reported on the psychosocial issues associated with the disorder as: depression, anxiety, apathy, resignation, irritability, agitation, hopelessness, decreased self-confidence, suspiciousness, and social isolation. Of the many psychological

problems individuals with PD experience, depression is the most common (Tandberg, Larsen, Aarsland, Laake, & Cummings, 1997).

Etiology of PD

The exact etiology of PD is unknown; however, in contrast to many other neurological disorders, the nature of the brain degeneration that causes PD has been well understood for decades. The symptoms of PD are caused by loss of nerve cells that secrete dopamine in the substantia nigra, which is in the basal ganglia region of the brain (Dakof & Mendelsohn, 1986). Typically, symptoms begin to develop after the degeneration of at least 80% of dopamine-producing neurons in the brain, which is directly related to the motor symptoms common in PD (Leader & Leader, 2001). Almost all of those who are diagnosed with PD are described as having idiopathic PD, meaning there is no specific known cause. In addition to idiopathic PD, symptoms which look very similar to PD but are less common may be related to familial PD, head trauma, cerebral anoxia, supranuclear palsy, or drug-induced PD (Di Monte, Lavasani, & Manning-Bog, 2002).

Onset and Diagnosis of PD

The onset of PD is insidious and the progression of the disease is gradual, which allows for it to go undetected for several years (Duvoisin, 1996). The age of onset for about 80% of PD cases occurs between the ages of 40 and 70 years old. There is a peak age of disease onset around 60 years of age (Jahanshahi & Marsden, 2000). 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).

Typically the diagnosis of PD is based on medical history and neurological examination, although it can be difficult to diagnose accurately, especially in the earlier stages. It is estimated that approximately 80% of dopamine producing cells in the brain are lost before the symptoms of PD appear (Duvoisin, 1996). Because early signs and symptoms of PD are often characterized as typical aging, physicians often need to observe patients for a period of time until it is apparent that the symptoms are consistently present (Gelb, Oliver, & Gilman, 1999). Early cardinal signs include shuffling of feet and lack of swing in the arms. Oftentimes brain scans or laboratory tests are requested to rule out other diseases; however, CT and MRI brain scans of people with PD can appear normal (Gelb, Oliver, & Gilman, 1999).

Treatment of Parkinson's Disease

Because of the chronic and degenerative nature of PD, it is a disorder that requires broad treatment and management, including patient and family education and support, wellness maintenance, physiotherapy, exercise, and proper nutrition in addition to the more standard medical treatments (National Institute for Health and Clinical Excellence, 2006). Although there is no present cure for PD, there are advances in psychopharmacology and surgical interventions that can provide some relief and/or reduction of symptoms.

Pharmacological treatment for PD began with the discovery of Levodopa (L-Dopa) in the late 1960s (Zillmer & Spiers, 2001). The primary goal of drug treatment is to improve the symptoms associated with PD and to increase the patient's quality of life. Still considered the best pharmacological treatment for PD, L-Dopa is metabolized in a

way that is converted to dopamine in the brain (Duvoisin, 1996). The result is an improvement in the symptoms for a brief period of time, with the effect wearing off and requiring additional doses. Individuals diagnosed with PD show variable response to L-Dopa, both in terms of the required dosage to see an effect, and the presence of side effects (Duvoisin, 1996). As with many medications, there are a number of side effects related to the use of L-Dopa. For example, with extended use, side effects such as disturbed sleep, perceptual illusions, and hypomania often develop (Zillmer & Spiers, 2001). Oftentimes other medications are needed to counteract the side effects of L-Dopa.

More recently, in the hopes of alleviating debilitating symptoms of PD, and because of the problems associated with the use of L-Dopa and other medications, newer surgical treatments have been developed as attempts to arrest disease progression and to subsequently improve motor functioning. The history of surgical intervention began in the 1950s when the first surgical procedures for the treatment of PD were performed (Côté, Sprinzeles, Elliot, & Kutscher, 2000). Because they were largely unsuccessful, they were discontinued until fairly recently when new surgical treatments were introduced based on greater understanding of the neurological processes of PD and the refinement of brain surgery techniques (Honey, Gross & Lozano, 1999). Three broad categories of surgical treatment for PD are ablation, or lesioning in certain areas of the brain, deep brain stimulation, and neural cell transplantation to the caudate and putamen in the brain.

The earliest surgical procedure for the treatment of PD involved creating surgical lesions in the basal ganglia in an attempt to disrupt the circuits in the brain that were

malfunctioning and causing the symptoms of PD (Côté, Sprinzeles, Elliot, & Kutscher, 2000). Although some of the patients who underwent this procedure improved, the surgery was imprecise, increasing the risk of damaging areas of the brain that were not involved in creating negative side effects in patients. Deep brain stimulation (DBS) involves implanting electrodes into the brain in order to alleviate the symptoms of PD. Similar to a pacemaker, the electrodes in DBS are attached by wires to a device underneath the skin in the chest, and they send electrical impulses to specific parts of the brain (Côté et al., 2000).

The third category of surgical procedures used to treat PD is neural tissue transplantation, which was the intervention used with participants in this study. This procedure involves the transplantation of fetal neural tissue into the striatum, an area of the basal ganglia that accepts dopamine from the brain stem (Borlongan & Sanberg, 2002). The theoretical basis for this surgery is the belief that fetal dopamine producing tissue will develop neural connections in the striatal tissue of the brain of patients with PD (Duvoisin, 1996). The goal is to increase the production and transmission of dopamine, thereby decreasing the symptoms of PD. There have been a number of clinical trials that have demonstrated that fetal tissue transplantation can improve some of the symptoms of PD and that the neurons that are transplanted can survive (Freed et al., 2001, Lindvall & Hagell, 2000, Betchen & Kaplitt, 2003, Björklund et al., 2003). Although there is relatively convincing data regarding the impact that transplantation surgeries can have on patients with PD, much less is known about how neural tissue

transplantation affects the long-term quality of life in individuals living with PD (McRae et al., 2004).

Quality of Life

Because of the severity, chronicity, and unpredictability of the physical symptoms, as well as the underlying psychological symptoms associated with PD, the quality of life (QoL) of patients with this disorder is greatly impacted. Individuals living with PD often have varied physical status and potential side effects due to their medications. For example, as the disease progresses, patients cannot predict how they will be functioning at any given time, and thus suffer from a loss of perceived control related to their mobility and ability to navigate their environment. Additionally, patients often feel embarrassed because of uncontrollable symptoms, which can cause social isolation and withdrawal. Oftentimes symptoms of depression and anxiety are connected to the changes in physical functioning as well as the decreases in interpersonal connection. As PD continues to progress, patients may suffer from a lack of physical and emotional energy to engage in social or leisure activities they previously enjoyed. This reduction in social contact has important implications for an individual's quality of life.

Although QoL has been defined in a variety of ways and includes a number of components, QoL in this study is focused on the broad categories of the physical, emotional, and social aspects of an individual's life. Physical well-being can be defined as perceived and observed bodily function or disruption (Cella, 1994). In PD, there are many factors that can potentially influence perceived and observed bodily function. Factors such as the specific symptoms of PD (tremor, bradykinesia, postural instability,

difficulty swallowing, poor voice quality, disruption of movement), side effects associated with the treatment of PD (inconsistent long-term effect of some medications, on-off syndrome, disturbed sleep), and the level of satisfaction with their medical treatment all play a role in the way a patient's physical functioning affects their QoL.

According to Cella (1994), emotional well-being as related to QoL reflects positive affect or an overall sense of happiness and contentment. The most common emotional difficulty reported by individuals living with PD is depression and anxiety, affecting approximately 40% or more diagnosed with PD (Rascol et al., 2003). Depression may occur more often in people with PD than among the general population, and is more commonly found in patients who are in the initial and later stages of PD (Cummings & Masterman, 1999). Similarly, anxiety also has a negative effect on the emotional well-being component of QoL. Anxiety has been related to increased psychosocial disability and decreased sense of emotional well-being in those living with PD (Menza & Dobkin, 2005). Individuals living with PD oftentimes experience anxiety due to the debilitating progression of the disease; anxiety also seems to become more severe once motor fluctuations develop (Menza & Dobkin, 2005). Studies have shown that there is often a comorbidity of depression and anxiety for those patients with PD (Shulman, Taback, Rabinstein, & Weiner, 2002).

The connection of social well-being to QoL involves perceived social support, maintenance of leisure activities, family functioning, and intimacy (Cella, 1994). Social support is a significant and fairly well recognized component of QoL and involves the maintenance of gratifying relationships with friends, as well as closer, more intimate

relationships with family members and significant others. For individuals with PD in particular, social functioning can often be dramatically affected by the disease. Because of the variability and unpredictability of side effects of medication treatment, patients are often concerned that the physical symptoms of the disease will become pronounced, resulting in social embarrassment. Rather than risk the potential public or social display of their symptoms, many patients avoid social situations outside of the home and gradually feel a loss of social well-being (Kuopio, Marttila, Helenius, Toivonen, & Rinne, 2000).

All three dimensions of QoL were of interest in this study. Thus, physical, emotional, and social functioning were all assessed. Additionally, optimism as defined by Moyer and colleagues (2008) as the way in which individuals perceive positive or negative experiences, was explored for its potential impact on well-being. It is hypothesized that these factors all contribute to the QoL of patients living with PD. There is little empirical information known about the effects of neural transplantation surgery in PD and its long-term impact on QoL for patients. In order to be able to understand which patients may benefit from this type of procedure, this study sought to better understand the longitudinal predictors of QoL in this sample. Additionally, virtually no information in the literature exists on the predictive factors of QoL for patients with PD undergoing this type of surgical treatment.

Optimism

Optimism has been related consistently to a variety of health-related outcomes across a broad range of conditions in the literature. In this study optimism was assessed in

order to determine the level of optimism relative to normative groups, as well as the impact of this variable on the QoL of participants in the study (Moyer et al., 2008). The Life Orientation Test (LOT), a commonly used measure, was used to assess dispositional optimism in this study (Scheier & Carver, 1985).

Statement of Purpose

Although there has been an established history that has explored and tested the various treatment interventions for individuals diagnosed with PD, there is less research on the exact effectiveness of fetal tissue transplantation as a treatment for PD. Additionally, even less is known about individual patient characteristics that may suggest that particular people living with PD may be good candidates for this specific procedure, and therefore likely to experience positive outcomes. Since the inception of neural tissue transplantation surgery as a treatment for PD, there have been empirical studies conducted in an effort to better understand and validate this procedure as an effective treatment; however, there is less of an understanding about the long-term effects of this type of treatment on the QoL of individuals living with PD. The present study addressed this important matter by exploring the longitudinal course of QoL among participants who underwent the surgical procedure from 12 to 15 years ago.

In particular, this study sought to examine the long-term aspects of QoL and functional impairment that are impacted by such a procedure. As fetal tissue transplantation surgery has continued to be explored as an option for treatment in the literature (Bjorklund et al., 2003), more is understood about the specific mechanisms of the procedure and the impact on primary physical symptoms of PD, but less is understood

about how a patient's overall QoL is affected. This specific distinction, due to a gap in the literature, allows for a unique contribution by investigating the status of patients who received this treatment 10 to 12 years after the surgery.

Quality of life has become fairly well addressed within the literature as a concept that ought to be included when attempting to fully and accurately understand the impact of medical illness and treatment interventions on patients. For individuals living with PD, because aspects of the disease significantly impact their physical functioning and limit their independence, many individuals experience problems with depression and overall decreases in their QoL. Quality of life has become a fairly broadly defined concept in the literature including many different factors such as physical functioning, occupational functioning, psychological well-being, sociability, and somatic comfort (Schipper & Levitt, 1985; WHO, 1958). One important contribution of this study is the ability to consider several aspects of QoL (physical, social, and emotional functioning) along with optimism in order to better understand the long-term effects of the surgery on these important outcomes.

As mentioned previously, treatment for PD has primarily focused on treating the patient's physical symptoms, therefore causing a lack of information related to how patients experience the impairments and limitations created by their neurological decline. More specifically, less information is known about how patients perceive the impact of their illness and its treatment on their well-being and social functioning.

More specifically, this study addressed a crucial and missing piece of understanding in the literature: what individuals seem to be doing well longitudinally

after this surgery versus those who appear to not be doing well, and importantly, why? Once a better understanding of the spectrum of improvement is established (e.g., can the sample be divided into "better" and "worse" groups?), another important question can be answered: can factors related to QoL or Optimism predict who will ultimately do well or not? 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).

Research Questions

1a. Among the participants in this longitudinal study, can patients be divided into two distinct groups of those who can be characterized as doing better and worse in terms of physical functioning, emotional functioning, social functioning, and optimism at the current assessment?

1b. If there are two groups, how does each group compare with the original sample that began the study in 1995 based on demographic variables and physical, emotional, and social functioning, as well as optimism at baseline?

2. What aspects of QoL (physical, emotional, social functioning) and optimism at baseline, are most predictive of those participants who are doing better and worse at the most recent time point?

Limitations of the Study

Several limitations exist in the present study. First, the sample size is small because it was drawn from the population in the original Parent Study, which had a small sample size (N = 40) due to the nature of the procedures involved. It was originally determined that a sample size of 40 would be sufficient to show a treatment effect due to

the fetal tissue transplantation surgery. Furthermore, the participants in this current study were drawn from the pool of 30 individuals who participated in the original QoL portion of the investigation. 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. Therefore, the total number of participants who were involved in the present study was small (n = 11).

Second, the findings from this study have limited generalizability to PD patients who do not meet the strict inclusion criteria that was established in the recruitment phase of the original study. Therefore, results are not applicable to patients with other neurological impairments or chronic diseases. This was a very unique study that involved experimental surgery and included the condition of sham brain surgery. It is probable that individuals who volunteered for this study do not represent the general population of persons with PD because of their willingness to undergo such an experimental procedure.

Summary

Chapter One presented an introduction to the definition and treatment history of PD. Included in this chapter was an overview of the physiology, onset, and symptoms associated with the disease as well as a specific discussion of the drug and surgical treatments. The concept of QoL was defined and introduced as a concept that is of importance and particularly relevant to individuals living with chronic illness, such as PD. 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, optimism, and QoL.

Chapter Two

Literature Review

Introduction

Chapter Two provides a review of literature related to several aspects of PD. Included in this section is a more detailed discussion of PD, and specific information on the various historic and current treatment options for individuals with PD. Because the focus of this study was on the longitudinal effects of neural transplantation of fetal tissue as a treatment for PD, more attention will be given to this surgical intervention. An extensive introduction to the broad concept of QoL, along with the components included in this study, are addressed, and the relationship between PD and QoL is discussed.

The literature reviewed in this chapter was identified in the following ways: 1) A computer search using the medical database, MEDLINE, was used to identify literature pertaining to this study. Search topics included QoL, placebo effect, surgical treatment of PD, treatment history of PD, and history of PD. 2) A second computer-assisted 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 both PD and QoL. 3) Additionally, reference lists of previously identified works and authors were examined in order to locate any additional publications relevant to the present study.

Definition of Parkinson's disease

Parkinson's disease (PD) is a chronic neurodegenerative condition for which there is no cure. PD was first discussed by a British doctor, James Parkinson, in 1817 when he described the "shaking palsy," which now bears his name (Clarkson & Freed, 1999). PD primarily affects movement and motor control, but can also lead to cognitive and psychological decline. The symptoms of PD develop after the degeneration of at least 80% of dopamine-producing neurons in the substantia nigra area of the brain (Leader & Leader, 2001). The degeneration of dopamine neurons in the substantia nigra creates substantial physiological disturbances in the basal ganglia, thalamus, and cerebral cortex of an individual's brain (Betchen & Kaplitt, 2003). The cause of degeneration in PD is unknown; however, it is known that the disease is not caused by behavioral, nutritional, or psychological characteristics of an individual. It is theorized that certain individuals may have a genetic susceptibility to developing PD, but there are many theories about the cause of PD that are currently under investigation.

Functional Impairment in PD

PD patients' physical symptoms include tremor, hypokinesia, rigidity, hypophonic voice, painful dystonia, postural abnormalities, gait disorders, sleep disturbances, depression, and drug related problems (Behari, Srivastava, & Pandey 2005; Shinder, Brown, Welburn, & Parkes, 1993). Frequently accompanying the motor symptoms directly related to PD are secondary physical, social, and psychological consequences such as falls, social embarrassment, depression, anxiety, dependence on

others for everyday activities, loneliness, and social isolation (Cummings, 1992; Richard, Schiffer, & Kurlan, 1996).

Due to increasing debilitation over time, persons with Parkinson's disease become less autonomous and more dependent on others for their care, often resulting in a reduction of quality of life for both the patient and the caregiver. With the majority of cases being diagnosed among those sixty years of age or older, as the population of older Americans increases, PD is becoming an increasingly larger concern for aging adults and society as a whole (American Parkinson's Disease Association; Menza, Marin, Kaufman, Mark, & Lauritano, 2004). Additionally, because of the increasing life expectancy in the United States, chronic diseases such as PD have received more attention and taken a leading role in health care (Schrag, Jahanshahi, & Quinn, 2000). Parkinson's disease creates many difficulties for the patient. As the disease progresses, the patient experiences physical limitations with increasing disability and impairment. Due to increasing debilitation over time, Parkinson's disease includes many symptoms that can result in a reduction of quality of life for both the patient and the caregiver.

Impact of PD on Patients

Patients with PD face not only the burden of the disease itself, but also the significant psychological burden of adjusting to the disease, which can compound its effects. Therefore, a growing trend in healthcare has shifted from the sole primary concern of managing physical limitations and treating the disease, to including the enhancement of health related quality of life (QoL; Martinez-Martin, 1998). The previous focus in the assessment of chronic neurological disorders such as PD was to document

and create changes in motor symptoms (Rahman, Griffin, Quinn, & Jahanshahi, 2008). Now that the physical consequences of PD have been well defined and documented, there has recently been a shift in the recognition that is placed on the importance of examining the impact of PD, including the medical/surgical treatments, on the daily life and psychological well-being of the patient.

Pharmacological Treatment of PD

Medical treatment and management of patients with PD has historically aimed at preserving life expectancy and limiting motor disabilities (Behari, Srivastava, & Pandey, 2005). There are two classes of pharmacological treatments used for PD: those medications that initiate the action of dopamine, and those drugs that work as dopamine receptor agonists, activating the dopamine receptors in the brain (Duvoisin, 1996). Dopamine replacement therapy is a historical treatment, which is known to alleviate some of the motor symptoms that occur early in the disease, but often fails to be effective as the progression of PD continues (Visser et al., 2008). This fact has expanded awareness that the clinical spectrum of PD is much broader, encompassing also many non-motor symptoms as described above.

Levodopa (L-Dopa) with a dopa decarboxylast inhibitor (DDCI), dopamine agonists, and monoamine oxidase B inhibitors have been the mainstays of typical PD treatment and drug therapy (Goetz, Poewe, Rascol, & Sampaio, 2005; Schapira, 2005; Schapira & Obeso, 2006). The discovery of L-Dopa occurred between the years of 1968 and 1970, and still remains the best and most widely used drug therapy for patients with PD (Clarkson & Freed, 1999; Schapira, 2005). L-Dopa generally proves effective as it

serves to replace the dopamine that becomes deficient as a result of PD. Although L-Dopa is the most widely used medication for the treatment of PD, it does have side effects such as inducing or increasing hallucinations in some patients, a lack of improvement for many disabling motor and non-motor symptoms, and the inability to stop the progression of PD (Clarkson & Freed, 1999l; Kaye & Feldman, 1986; Rascol, Payoux, Ory, Ferreira, Brefel-Courbon, & Montastruc, 2003).

The Parkinson Study Group (2004) created a study to evaluate the effectiveness of L-Dopa on the progression of PD. In this study, 361 patients with PD who had never received dopaminergic medications before were randomly assigned to one of two groups: placebo or L-Dopa. Those patients who were in the L-Dopa group either received 150, 300, or 600mg/day for 40 weeks, followed by a two week period off all medications. The Unified Parkinson's Disease Rating Scale (UPDRS; Fahn & Elton, 1987) was used to assess symptoms of functional impairment in both groups. The UPDRS showed higher levels of depression for those in the placebo group. There was a decrease in UPDRS scores for those participants in the highest L-Dopa dosage group; however, dyskinesias were commonly found in this group (The Parkinson Study Group, 2004).

The emergence of dyskinesias due to L-Dopa is believed to be related to the difficulty of storing the drug in the brain due to the loss of the dopamine terminals there (Jankovic, 2006). This is thought to cause dyskinesias due to a lack of continuous delivery of the drug to the brain. In patients with more advanced PD, who experience motor fluctuations such as dyskinesias, the addition of a catechol-O-methyl transferase

(COMT) inhibitor reduces off-time and increases on-time by extending the half-life of levodopa (Widness & Comella, 2005).

Several limitations of pharmacological treatment of PD exist. Currently, L-Dopa therapy proves beneficial for several years; however, PD continues to progress and the body attenuates to its use, rendering it less and less effective over time. Additional medications often given to treat the side effects of L-Dopa may result in the patient having to manage the administration of several medications throughout the day, which can become burdensome. The inability of drug therapy to halt the progression of PD and restore adequate motor functioning in patients with PD has led to a search for alternative treatments, including surgery (Clarkson & Freed, 1999).

Surgical Treatment of PD

The development of surgical treatment for PD began in the 1930s in an effort to alleviate the devastating symptoms associated with the disease (Duvoisin, 1996). Various ablative procedures were performed initially with the idea that if the motor pathways were damaged enough, the motor symptoms such as tremor and rigidity may diminish (Cowley, Murr, Peyser, & Sawhill, 2000). During this specific procedure, brain tissue affected by PD was located and then destroyed in an effort to restore healthy chemical and electrical impulses (Cowley et al., 2000). This was a fairly dangerous technique that produced unpredictable results, carrying a significant risk of damaging surrounding brain tissue (Duvoisin, 1996).

Continued surgical advances produced a technique known as stereotactic surgery, which involved inserting a needle into the striatal area of the brain (Duvoisin, 1996). This

early procedure involved the administration of alcohol, electric current, or liquid nitrogen in an effort to destroy the area of the brain associated with the motor symptoms. In 1948, stereotactic techniques were adapted and considered less dangerous than ablation, but there was still concern and controversy in the neurological community about the use of these techniques (Duvoisin, 1996). The symptoms of tremor and rigidity were relieved only temporarily with sterotactic surgery, and there was considerable risk of stroke. Ultimately, these early forms of surgical intervention for PD became less frequently used and were restricted to only a few patients with PD as better knowledge of the areas of the brain that play an active role in PD symptoms emerged.

Researchers have well documented that the subthalamic nucleus (STN) and the globus pallidum internus (GPi) areas of the brain are most directly related to the motor symptoms associated with PD (Jankovic, 2006). From 1981 to 1984, an initial experimental procedure was performed in Stockholm, Sweden, in which dopamine-producing nerve cells were transplanted from the adrenal medulla of fetal animals into the brains of humans (Goetz et al., 1989). There were mild improvements in symptoms to some patients; however, there were also serious complications and sometimes death as a result of this new procedure. The resulting theory that came out of this phase of surgical treatment was that damaged brain tissue was stimulated by the chemical release of a growth factor that corresponds to the development of dopamine fibers in the damaged area (Duvoisin, 1996).

Deep brain stimulation (DBS) surgery emerged from many of the historical and experimental surgical treatments for neurological disorders such as PD. DBS is the

application of implantable electrical stimulation technology and devise to treat neurological disorders (Coffey, 2008). During DBS surgery, electrodes are implanted into the brain of a patient and, several days later, a pacemaker is implanted into the chest of the patient and adjusted to the correct settings to control the electrodes (Krack et al., 2003). DBS influences brain function (movements, sensations) and behavior (thoughts and feelings) in a way that can relieve symptoms and improve the overall functioning of the patient (Coffey, 2008). Investigators in the first half of the 20th century applied electrical stimulation to intracerebral targets within the limbic forebrain, thalamus, hypothalamus, basal ganglia, and the brain stem in experimental animals. Effects were observed that sometimes outlasted the duration of the stimulation and included affective, aversive, analgesic, autonomic, and behavioral changes (Delgado, 1961; Heath & Mickle, 1960). By the late 1980s, DBS began to emerge as a potentially life-changing therapy for patients with medically intractable involuntary movement disorders such as PD (Coffey, 2008).

Jankovic (2006) conducted a double-blind study of 143 patients with advanced PD. DBS was performed and results suggested that motor scores of the treatment group improved by 49% when compared to those who did not receive DBS. A six-month follow-up was conducted and those who received DBS showed an improvement in "on" time without dyskinesias. There were however, significant side effects of the DBS, including intracranial hemorrhage in seven of the participants, with no significant change in speech over time. Researchers concluded that STN DBS did not appear to be better

than L-Dopa drug therapy, but DBS was believed to improve motor side effects related to taking L-Dopa (Jankovic, 2006).

As outlined above, there have been a variety of neurosurgical operations that have been proposed and performed for the treatment of PD. The surgical treatment history of PD includes destructive lesioning of the thalamus and pallidum, chronic deep brain stimulation, and more recently efforts have been focused on neural transplantation (Clarkson & Freed, 1999). The goal of neural transplantation in PD is to increase the production and transmission of dopamine directly into the striatum (Date & Ohmoto, 1999). The hope of this surgical treatment for PD is that the transplanted cells will establish dendritic connections with the patient's existing dopamine receptors, resulting in normalization of the production and transmission of dopamine (Fazzini, 1993). Prior to neural transplantation in human patients with PD, successful laboratory studies of embryonic dopamine cell grafts in parkinsonian animals were conducted and eventually became the groundwork for proceeding with clinical trials of neural transplantation therapy in humans (Borlongan & Sanberg, 2002).

The clinical trials of fetal cell transplantation as a treatment for PD have developed in two separate phases. In 1987, a series of small open-label trials were initiated to obtain evidence to support the viability of transplantation as a therapy for PD (Bjorklund et al., 2003). These early trials showed unequivocally that human fetal dopaminergic neurons can survive and function for more than 10 years in the striatum of patients with PD and provided a clear indication that grafted fetal dopaminergic neurons can be therapeutically effective (Dunnett, Bjorklund & Lindvall, 2001). Based on the

results of these trials, the National Institutes of Health (NIH) decided to support a second phase; where two double-blind sham-surgery controlled trials were launched in the early 1990s (Freed et al., 2001; Olanow, 2002).

For transplant surgery, dopamine cells from human fetal ventral mesencephalon has been shown to be the preferred tissue for transplantation into human PD patients (Bjorklund et al., 2003), although clinical use of human fetal tissue has created ethical as well as scientific and logistical problems. Because of these concerns, the supply of human fetal tissue is limited and variable in quality. There are oftentimes difficulties accessing an ample supply of disease-free and homogenous dopaminergic cells, therefore causing some researchers to use transplanted fetal pig neural cells (Borlongan & Sanberg, 2002; Cesario & Sanberg, 2002; Clarkson & Freed, 1999).

Because the Parent Study, on which the present study is based, involved participants who received fetal tissue transplantation surgery, the remainder of this section will focus on this specific treatment.

The efficacy of fetal tissue transplantation surgery for reducing the symptoms of PD has been investigated since the surgery began in the 1980s (Clarkson & Freed, 1999; Clarkson, 2001; Freed et al., 1992). In an effort to improve the results following fetal tissue transplantation, Freed et al. (1992) piloted an experiment with seven patients with PD, where embryonic tissue was implanted into their striatum. Immediately following surgery the results were promising with improvement in physical symptoms associated with PD as well as patients' functional abilities; however, the efficacy of the procedure

was clouded by the lack of a control group and questions related to the placebo effect (Freed et al., 1992).

In 2003, a study was conducted in which 34 patients with PD received fetal tissue transplantation and were followed during a 24-month double-blind, placebo control trial (Olanow et al., 2003). Although there was no significant difference in improvement between the treatment and control group, they did find a significant benefit of the transplant for those patients who had less severe motor symptoms prior to surgery. In other words, the researchers were able to conclude that the fetal transplantation procedure did not improve motor symptoms for patients, but it was able to prevent further decline of such symptoms (Olanow et al., 2003).

The Parent Study: Fetal Tissue Transplantation

The Parent Study, from which the current study is derived, is part of the continued research on the transplantation of human embryonic dopamine neurons in the patients with PD. Freed et al. (2001) conducted a double-blind sham controlled trial to investigate the effectiveness of fetal tissue transplantation into the brains of individuals suffering from advanced stages of PD. Forty individuals with severe PD between the ages of 34 to 75 were randomly assigned to receive a transplant of embryonic dopamine neurons or undergo sham surgery. All patients were told that if assigned to the sham surgery group, they would have the option of receiving the transplant surgery at the conclusion of the study. Regardless of treatment condition, participants were followed in a double-blind approach for one year.

The procedure for those individuals who were assigned to the transplant group was that cultured mesencephalic tissue from four embryos was implanted into the putamen area of their brain. Participants who underwent the sham surgery had holes drilled into the skull, but the dura was not penetrated. Additional information regarding the surgical procedure can be found in the original Parent study article (Freed et al., 2001). Results of this study suggest that the age of the participants was related to their medical outcome. Younger patients, who were under the age of 60, showed significant improvement on the outcome measures of PD in the transplantation group as compared with the sham surgery group when patients were tested in the morning before receiving their medication. No significant improvement was found in older patients in the transplant group. The researchers concluded that human embryonic dopamine neuron transplants survived in patients with severe PD; however, any clinical benefits of the treatment depended on the age of the patients (Freed et al., 2001).

Results of the Original Quality of Life Study

The original QoL study, upon which the present study is based, investigated the QoL of patients in both the transplant and sham conditions (McRae et al., 2004). Quality of life was assessed in patients at several time points (baseline, 4, 8, and 12 months after surgery) during the one-year double-blind follow up. In addition to assessing QoL, the study explored treatment outcomes based on the treatment group the patients *perceived* that they were in (transplant vs. sham). Results of this study indicated differences over time between the actual transplant and sham surgery groups. The only statistically significant difference between the transplant and sham surgery groups was in the area of

social contact at 4 months, with the sham surgery group reporting more social contact. Additional analyses revealed there was a change across time, with a significant improvement in physical functioning in both treatment groups over the 12 months following the surgery.

Secondary results of this study were related to perceived treatment groups, or the type of surgery patients thought they received at each of the time points. Several differences between perceived treatment groups existed, all of which were in favor of the perceived transplant group. Participants who believed that they had received the transplant reported more positive results regarding QoL than those who believed they received the sham surgery. Additionally, an interesting finding confirmed the presence of the same effect across the evaluations of the medical staff. In other words, there was a very strong placebo effect not only for the patients in this study, but also for the objective medical staff.

Definition of Quality of Life

Quality of life (QoL) has become an important construct in the assessment and treatment of Parkinson's disease (PD). Although capturing the subjective experience of patients and incorporating the effect of a disease and its treatment on an individual from his/her own point of view is now widely accepted, there exist many definitions and understandings about what constitutes QoL. In general, definitions of QoL emphasize that it "is in the eye of the beholder." QoL represents subjective evaluations of oneself and of one's social and material world and reflects the extent to which the individual is

satisfied with, or is bothered by problems in those areas (Den Oudsten, Van Heck, & De Vries, 2007; Orley, Saxena, & Herrman, 1998).

The World Health Organization Quality of Life Group (WHOQOL Group; 1995) defined QoL as, "an individual's perception of his/her positioning life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards, and concerns" (p. 1405). This operational definition of QoL is broad and incorporates the person's physical health, psychological functioning, level of independence, interpersonal relationships, individual beliefs, and their relationship to relevant features of the environment (WHOQOL group, 1995).

Dimensions of Quality of Life

Quality of life can incorporate a number of specific variables, which can be subsumed under several domains such as physical functioning, emotional well-being, and social support. Kaplan, Anderson, Wu, Mathews, Kozin, & Orenstein (1989) used the term health-related quality of life to refer to the impact of health conditions on function but included social well-being as well. Martinez-Martin (1998) specified that QoL measures should consider physical status and functional ability, psychological status, social interactions, economic and vocational status, and religious and spiritual status.

HRQoL is more specific as it refers to the impact of health conditions on overall functioning (Kaplan, Anderson, Wu, Mathews, Kozin, & Orenstein, 1989). In clinical medicine, QoL refers to the patient's own perception and self-evaluation regarding the effects of an illness and its consequences on his or her life (Martinez-Martin, 1998).

Some researchers have proposed the related concept of health-related quality of life (HRQoL) in order to narrow the definition of QoL. HRQoL focuses on QoL in relation to the impact of a disease and treatment on patients, the physical, emotional, and social well-being after diagnosis and treatment, and also includes a combination of objective functioning and subjective perceptions of health (Curtis & Patrick, 2003; Kaplan, 1985; Testa & Simonson, 1996). Therefore, HRQoL is incorporated into the above definition of QoL, although it is less broadly formulated.

In addition to HRQoL, perceived health status (HS) has been identified by researchers as a separate, but related construct in an effort to tease out the different types of patient-based outcomes. HS refers to perceived health in terms of physical and mental symptoms and social conditions or functions, but not in terms of internal experiences (Den Oudsten, Van Heck, & De Vries, 2007). Specifically, HS represents the impact of health on one's ability to perform a variety of physical, social, and emotional activities (De Vries, 2001). In comparison, QoL represents reflections of the way in which patients "perceive and react to their health status and to other, non-medical aspects of their lives" (Gill & Feinstein, 1994, p. 619). Therefore, HS is a factor that may influence HRQoL, and could be thought of as a possible predictor of HRQoL, but not as a part of it (Den Oudsten, Van Heck, & De Vries, 2007).

Given the separate distinctions in definition, it is believed that QoL should not be used as an umbrella term for various desired patient medical outcomes (Patrick & Erickson, 1998). Specifically, HS refers to levels of functioning, while QoL and HRQoL reflect internal experiences (Curtis & Patrick, 2003; De Vries, 2001; Den Oudsten, Van

Heck, & De Vries, 2007). Consequently, HS measures contain items about actual patients' functioning (e.g., "Due to Parkinson's disease, how often did you have problems walking half a mile?"), HRQoL measures focus on the subjective evaluation of health (e.g., "How satisfied are you with your abilities?"), while QoL measures exceed the health domain by focusing on the subjective evaluation of life as a whole (e.g., "How would you rate your overall quality of life?"; Den Oudsten, Van Heck, & De Vries, 2007).

Quality of life has been widely recognized as a vital aspect of determining the effectiveness of interventions and treatment. In other words, the medical and scientific community has moved towards validating the importance of assessing not only the physical and neurological aspects of change and improvement affected by a treatment, but are now also interested in knowing how the intervention affected patients' and caregivers' lives as well (Behari, Srivastava, & Pandey, 2005). An important aspect of QoL that distinguishes it from earlier assessments done in the treatment of PD is that it incorporates the patient's own perspective of his/her general health and well-being, as mentioned above. Therefore, the importance of the patient's perspective in addition to objective medical assessments has been accepted as well.

The concept of QoL has often been considered to be related to the duration of life; however, it can also more importantly be thought of as primarily relating to the condition of life, regardless of duration. Martinez-Martin (1998) has noted "people want to live longer, but they also want to live better" (p. 2). Therefore, a sense of well-being is at the core of the concept of QoL. As the operational definitions above describe, there is

acceptance that QoL is a multidimensional concept that encompasses the physical, emotional, and social components associated with an illness or treatment (Schrag, Jahanshahi, & Quinn, 2000). In clinical medicine, QoL refers to the patient's own perception and self-evaluation regarding the effects of an illness and its consequences on his or her life (Martinez-Martin, 1998).

Importance of Quality of Life

As mentioned previously, the treatment of Parkinson's disease (PD) is primarily focused on improving a patient's motor function although recently, non-motor symptoms have been recognized as being potentially problematic, affecting the QoL of patients with PD. However, in the advanced stages of the disease, patients often experience additional difficulties, such as treatment related complications, falls, depression, and dementia, which may have a much greater impact on the patients' QoL than the cardinal features of Parkinson's disease (Schrag, Jahanshahi, & Quinn, 2000). It has been noted that many factors that are important to patients, such as emotional and psychosocial consequences of their illness, are usually omitted from a physician's assessment of the patients' progress (Martinez-Martin, 1998). In order to best assess these factors in PD, QoL is often thought of as a multidimensional concept, as noted above, encompassing not only the patient's physical well-being but also the patient's emotional and psychological well-being.

Assessment of any sort must be considered in terms of its practical utility and importance for the scientist and the practitioner. What is the value of addressing this issue? Is it worth the time it takes to ask questions or administer a QoL instrument? How will it help the practitioner to provide better care for the patient and/or family? There are

several critical answers to these questions. In regard to interventions, it is important to determine whether a particular treatment improves status not only in terms of UPDRS scores, for example, but also in terms of practical outcomes in patients' lives. Health-care providers must often consider the costs and benefits of treatment not only in terms of physical risks and financial expenses, but also in terms of "quality of life" benefits for patients. Further questions include, "For whom is this treatment helpful?" "What are the possible side effects of treatment?"

Considering QoL is also important in determining whether adjunctive treatments may be helpful for patients and families coping with PD. If quality of life is "poor" in spite of the best neurological care and adjustment of medications, medical personnel may want to consider what can be done to improve the patient's situation. What supplementary medications (e.g., for depression) or therapies (e.g., psychosocial interventions, groups, physical therapy) might be suggested to improve overall patient functioning and QoL? The rationale is that if the "whole person" is addressed, not just the medical and neurological status of the patient, the actual response to medication and treatment may be improved.

One consideration in regard to QoL is that contributors to better life quality may vary among different age groups. For example, young-onset PD patients may regard continuing to work and enjoying their careers as a great value, whereas a patient who has already retired has other interests and concerns. Likewise, a younger patient may care deeply about staying well longer for the sake of his or her children and being able to continue in the role of contributing spouse and parent. An older patient may focus on

remaining well enough to continue living independently without having to go to an assisted-care facility. Thus, it is important to consider aspects of age when assessing QoL as, many times, one way of assessing the construct does not fit all circumstances or does not address the varying values and goals of all individuals. Awareness and sensitivity to unique aspects of a patient's life situation are critically important.

Quality of Life and Depression

Depression is widely recognized as a major psychological component of PD and is the most common neuropsychiatric disturbance found in patients with the disease (Menza et al., 2004). It is more frequently found in individuals with PD than in the general population or with any other chronic illness (Jones, Pohar, & Patten, 2009). It is difficult to determine whether depression is a response to the diagnosis and ongoing progression of the disease, or whether it is physiologically a part of the disease. It may be either or both, perhaps depending on the person, the amount and quality of social support available to the person, the patient's financial status, and a multitude of other factors (Pontone et al., 2009).

Although the reported prevalence for depression varies depending on the methodological implications of various studies, approximately 40% is the statistic that is generally accepted, with one-half of the patients with PD meeting criteria for major depression and one-half meeting criteria for dysthymia (Cummings, 1992; Menza et al., 2004). Depression is of significance in individuals living with PD because, in addition to the personal suffering and decline in functioning they experience, their depression is also associated with a faster progression of physical symptoms, greater decline in cognitive

skills, and greater decline in the ability to care for oneself (Brown, MacCarthy, Gotham, Der, & Marsden, 1988; Cummings, 1992; Menza et al., 2004; Starkstein, Mayberg, Leiguarda, Preziosi, & Robinson, 1992).

Depression in individuals with PD along with the mental health impairments is clearly associated with lower QoL as well as other health behaviors (Jones, Pohar, & Patten, 2009). Depression and other non-motor symptoms have been shown to have significant impact on QoL. Several studies have found that depression is one factor that may be more burdensome than the motor symptoms of PD (Schrag, Jahanshahi, Quinn, 2000; Schrag, Jahanshahi, Quinn, 2000).

Quality of Life and Anxiety

Similar to depression, anxiety is another common and disabling complication of PD that is not considered a primary or physical symptom. The presence of an anxiety disorder in persons with PD oftentimes causes increased disability and worse QoL (Carod-Artal, Ziomkowski, Mourao, & Martinez-Martin, 2008). While patients with PD seem to experience conditions such as Generalized Anxiety Disorder (GAD), panic disorder, and phobias, the anxiety problem that is most unique to PD patients include anxiety associated with fluctuations in motor symptoms (Pontone et al., 2009).

There have been several studies devoted to exploring and better understanding the prevalence and consequence of anxiety in patients with PD. In one study, 28% of individuals living with PD had a formal anxiety disorder diagnosis and an additional 40% had anxiety symptoms (Menza, Robertson-Hoffman, & Bonapace, 1993). A recent study found that the general prevalence of anxiety disturbances in individuals with PD was

40%, a rate that is markedly higher than in both healthy and comparably disabled elderly populations (Nuti et al., 2004; Pontone et al., 2009). Additionally, there is significant comorbidity that occurs for patients of PD who have both depression and anxiety. In the same study, Menza and colleagues (1993) found that, of those patients with PD who have been diagnosed with depression, 67% also met criteria for an anxiety disorder. Anxiety has been found to be a significant determinant in the QoL of patients living with PD (Carod-Artal, Ziomkowski, Mesquita, & Martinez-Martin, 2008).

Quality of Life and Optimism

Individuals living with PD oftentimes experience psychological consequences of the disease such as depression and anxiety, which affect their QoL as mentioned above. Other factors such as optimism have been found to be associated with health-related quality of life for individuals living with PD and other chronic illnesses (Koplas, Gans, Wisely, Kuchibhatla, Cutson, Gold, et al., 1995; Zenger, Brix, Borowski, Stolzenburg, & Hinz, 2010). Optimism and pessimism have been reported as important dimensions to study in chronic medical conditions such as PD (Gruber-Baldini, Ye, Anderson, & Shulman, 2009).

Previous studies have investigated the role of optimism in disability and QoL, specifically in patients living with PD. Shifren (1996) conducted a longitudinal study of optimism and disease severity with a sample of 12 individuals diagnosed with PD. The results of that study did not find any significant relationship between disease severity and optimism; however, The Global Parkinson's Disease Survey (2002) did find a statistically significant impact of optimism on health-related QoL in 902 PD patients. Results of a

study with a smaller sample of individuals with PD found that higher levels of optimism were associated with better mental health factors related to QoL, but were not found to be related to level of disability associated with PD (Gruber-Baldini, Ye, Anderson, & Shulman, 2009). A longitudinal study of patients diagnosed with urogenital cancer found that optimism at baseline was predictive of health-related QoL outcome measures three months later (Zenger, Brix, Borowski, Stolzenburg, & Hinz, 2010).

Summary

Chapter Two included a literature review of more specific information on PD, pharmaceutical treatments and surgical interventions, specifically, fetal tissue transplantation. A more detailed discussion of QoL was also included in Chapter Two. The present study was designed to investigate the current level of QoL for those individuals living with PD who participated in the Parent Study 10-12 years ago and received fetal tissue transplantation surgery. This study will explore what participants seem to be doing better at the most recent time point, based on the three aspects of QoL: individuals' Physical, Emotional, and Social functioning and a measure of Optimism.

Chapter Three

Method

This chapter describes the methodology used to address the research questions in this study. Descriptions of the participants, measures, and data analyses are included.

Participants

Forty individuals with advanced Parkinson's disease (PD) were recruited to participate in a double-blind surgical trial, referred to as the Parent study (Freed et al., 2001). The average age of participants in the Parent study was 55.9. Average duration of disease was 15.7 years with an average age at onset at 42.1 years of age. There were equal numbers of male and female participants; 91% were Caucasian and the average number of years of education was 16.2. Of those participants, 20 were randomly assigned to receive the fetal tissue transplant and 20 patients were assigned to the sham surgery condition.

The participants in the Parent study were all invited to participate in an additional quality of life study (QoL); 30 patients agreed. The average age of participants in the QoL study was 57.8. Average duration of disease was 13.57 years. There were equal numbers of male and female participants and nearly 87% of them were Caucasian. The average number of years of education for the participants in the original QoL study was 16.4.

Of the 30 participants in the original QoL study, 14 individuals were able to be contacted and invited to participate in this follow-up study, and subsequently 11 agreed to be included in the current study. The average age of participants in the current study was 51.9. The average duration of disease for this population was 13.64. There were more females than males who participated in the follow-up study (females = 8, males = 3), and 100% of this sample was Caucasian. The average number of years of education in this follow-up sample was 16.8.

Inclusion Criteria

The inclusion criteria for the participants to be accepted into the Parent Study (Freed et al., 2001) were: 1) advanced stage of idiopathic PD of at least 7 years duration with responsiveness to L-Dopa; 2) continued but diminished improvement from L-Dopa, which equaled 33% improvement in the sum of the total scores on the UPDRS; 3) patients previously tried on other available forms of medical treatment; 4) presence of an intractable problem, such as "off" periods, dyskinesias, or "freezing," not controlled by dopamine agonists; 5) medically fit to undergo transplant surgery with certification by the patient's physician; 6) commitment to actively participate in ongoing research and demonstrate an ability to pay for expenses not covered by the initial NIH grant for the original Parent Study; 7) age range between 20 and 75 years; 8) no serious depression, hallucinations, or cognitive impairment; 9) normal MRI scan of the brain within the last 18 months; and 10) fluorodopa PED scan compatible with idiopathic PD.

Exclusion Criteria

The exclusion criteria for the participants involved in the Parent Study included: 1) severe or moderately severe depression; 2) gross signs of dementia, as this could indicate the existence of concurrent Alzheimer's disease or diffuse Lewy body disease, which would interfere with the ability of the examiners to adequately test the subject; 3) previous brain surgery, injury, or exposure to toxins; 4) presence of diabetes mellitus, severe cardiopulmonary disease, or other severe medical disease; 5) taking neuroleptic medication; and 6) not medically cleared to undergo a surgical procedure (Freed et al., 2001).

Procedure

Contact information for the 30 patients who agreed to participate in the original QoL study was used in an attempt to communicate with them regarding the current study and their willingness to participate. For those individuals who were not able to be reached based on the contact information obtained from the researchers of the original QoL study, the internet was used in order to attempt to locate current contact information for all 30 participants. Of the 30 participants, 14 individuals were able to be reached, updated their contact information (i.e., phone number, address, etc.), and therefore were sent an invitation to participate in this follow-up study. Participants were contacted via telephone and information was provided to them about the current study and their willingness to participate was assessed.

Current data related to participants' physical functioning and PD, as well as quality of life variables, since the original study concluded, were gathered through

questionnaires that were sent through the mail. Of the 14 individuals who were sent questionnaires, 11 completed and returned them in the postage paid envelope that was provided. Follow-up phone calls were made to the remaining three participants to confirm that they received the mailing, determine if there were any problems, and to encourage their participation by returning the questionnaires.

Once the questionnaires were received from participants, the data were aligned in order to assess the longitudinal nature of each participant's data. Because of the nature of the original Parent study, there were two different groups of participants: those who initially received the transplant and were assessed at baseline, 12, and 24 months in "real time," and those who initially received the sham surgery, were assessed at baseline, 12, and 24 months, but then elected to receive the transplant once the blind was lifted at 12 months, and were subsequently assessed at 12 and 24 months after the transplant. Therefore, the data for the initial sham group were shifted so that the time points for all participants were equivalent: baseline (pre-surgery), 12 months, and 24 months after surgery and then the most current data obtained. Therefore, trajectories and predictions across time were able to be explored.

Measures

A variety of widely recognized instruments were used to create composite variables focusing on three fundamental domains that make up QoL: Physical functioning, Emotional functioning, and Social functioning. In addition, a number of variables thought to be related to quality of life and potential predictors of QoL were also

assessed. These variables included optimism, and the specific demographic variables of age, gender, and duration of illness.

Demographics. Participants were asked to report their age, gender, level of education (in years), ethnicity, employment status and income, marital status (including number of years married) and living situation. Additional demographic information was obtained regarding duration of illness and age of onset of PD diagnosis.

Physical Functioning

Each participant's level of physical functioning was measured using the compilation of several recognized measures for patients with PD: the Unified Parkinson's Disease Rating Scale (UPDRS) adapted for patients (Montgomery, Lieberman, Singh, & Fries, 1994), the Hoehn and Yahr Stage of Disease scale (Hoehn & Yahr, 1967), and the Schwab and England Activities of Daily Living scale (Schwab & England, 1969).

The Unified Parkinson's Disease Rating Scale (UPDRS) is a widely used clinical tool that assesses motor functioning and the degree of functional impairment caused by PD (Fahn & Elton, 1987). The original version of this scale is scored by medical personnel, and is the most widely used assessment of motor function in PD (Fahn & Elton, 1987). The patient version of the UPDRS was adapted from the original version in order for patients to provide their own subjective ratings of their level of functioning and used to measure the longitudinal course of PD in participants in the current study (Montgomery, Lieberman, Singh, & Fries, 1994).

Four subscales comprise the UPDRS: Activities of Daily Living (ADL's) at "Best" and "Worst" and Severity of Symptoms at "Best" and "Worst." The subscales of

ADL's at "Best" (when patients are physically "at their best") and "Worst" (when patients are physically "at their worst") are each comprised of eight items that are scored from 1) Normal, 2) Adequate, 3) Limited, 4) Need Help, to 5) Unable to do. Each scale is scored separately and scores represent the patient's level of functioning when they are at their "best" and at their "worst." The possible range in scores for each scale is 8 to 40, with higher scores indicating more debilitation and lower scores indicating more independence in activities of daily living. Items include walking, dressing, cutting food, hygiene, getting up from a chair, turning in bed, writing and talking.

The subscales of Severity of Symptoms at "Best" and "Worst" are each comprised of five problems, which the patient rates at his/her "best" functional level and at his/her "worst." Each item is rated on the following Likert scale: 1) Normal, 2) Mild, 3) Moderate, 4) Severe, and 5) Very Severe. The range of total possible scores is from 5 to 25, with 5 indicating "normal" and 25 indicating "very severe" in all areas. Higher scores indicate more debilitation. The five problems listed include: tremor, swallowing, salivation, "freezing" when walking, and falling.

Reliability for the subscales on the patient version of the UPDRS ranged from .65 to .90 (McRae et al., 2004). The original UPDRS has demonstrated acceptable construct validity across other widely used measures of physical functioning in PD (Ramaker, Marinus, Stiggelbout, & van Hilten, 2002).

An additional single item was also used to assess the level of physical functioning related to QoL. The *Free or Restricted Scale* is a single, global item that measures how free or restricted the person feels "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, with lower scores suggesting better functioning.

Stage of Parkinson's Disease. The patient's stage of disease was assessed using a version of the Hoehn and Yahr scale (Hoehn & Yahr, 1967), the standard measure of disease severity in PD. This version of the scale was adapted specifically for use by patients and has been shown to correlate well with neurologist ratings (tau-b = 0.73, $P <$ 0.001; McRae et al., 2002). Descriptions of each stage were provided on the questionnaire and standard ratings ranging from 0 (no signs of disease) to 5 (wheelchair bound or bedridden unless aided) were used.

The Severity of Problems 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."

Functional Activity Level. The Schwab and England Activities of Daily Living scale (Schwab & England, 1969) was designed specifically to evaluate the level of functioning related to activities of daily living among persons with PD. This scale has been used in numerous research studies with this population (Goetz et al., 1989). The scale ranges from 100% (completely independent) to 0% (bedridden), with each 10% increment having specific definitions. Although designed for use by physicians, this scale has been shown to have high inter-rater reliability between patients, caregivers, and

neurologists (McRae, Diem, Vo, O'Brien, & Seeberger, 2000). Patients in this current study rated themselves using the scale at each of the four assessment periods.

Emotional Functioning

Depression. Dysphoric mood and depressive affect related to QoL was measured with the Center for Epidemiologic Studies Depression Scale (CESD; Radloff, 1977). Importantly, the CESD is a measure of depressive symptoms and mood rather than a measure of diagnosable illness or disorder (Ensel, 1986). 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 (less than one day) to 3 (5-7 days), with total scores ranging from 0 to 60. A score of 16 is often regarded as a cut-off point for the presence of clinical symptoms of depression (Burker et al., 1995). Participants were asked to indicate how often they had experienced each item or symptom during the past week. Lower scores indicate less depression. Items such as, "My sleep was restless" and "I was happy" are designed to assess depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, loss of appetite, sleep disturbance, and psychomotor retardation (Hughes, Demallie, & Blazer 1993).

Based on the original study, internal consistency (Cronbach's alpha) for the CESD was found to be .89 (Radloff, 1977). Test-retest reliability was found to be acceptable. Radloff (1977) 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 Bergman (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, DeMallie, and Blazer (1993), CESD scale items have been shown to have satisfactory internal consistency, acceptable test-retest stability, good concurrent validity, and adequate construct validity.

Anxiety. The State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) was developed to assess two types of anxiety: current, situational aspects of anxiety as well as more long term "trait" levels 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 found 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).

Stress. The Parkinson's Disease (PD) Stress Scale was developed to be administered 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 causes them considerable stress, or clearly bothers 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 Intrusiveness of Illness Scale is a 15-item scale that measures the degree to which a chronic illness interferes with usual life activities (Devins et al., 1984). The range of responses for individual items is from 1 (very little) to 7 (a great deal). Lower scores indicate less intrusiveness. A total score on the Intrusiveness of Illness Scale can range from 15 to 105 (Devins et al., 1984). Examples of items include, "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 et al., 1984). 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

Perceived Social Support. The Social Provisions Scale (Russell & Cutrona, 1987) is a 24-item scale designed to measure the extent to which an individual perceives that his/her current relationships provide the six social provisions described by Weiss (1974). Each item is rated on a 4-point scale ranging from 1 (strongly disagree) to 4 (strongly agree). Previous research has found reliability estimates (coefficient alpha) ranging from .65 to .76 on the subscales measuring each of the social provisions. Reliability of the total Social Provisions score was estimated to be .92 (Cutrona & Russell, 1987). Validity has been established in a number of different studies (see review by Cutrona & Russell, 1987). After reverse scoring 12 items, total scores could range from 24 to 96, with higher scores indicating more perceived social support. The SPS has been used with previous samples of PD patients as well as caregivers of PD patients (McRae & Bowles, 1992**;** McRae & Sherry, 1991; McRae, Cherin et al, 2004). Results of these studies indicated that both patients and caregivers reported similar levels of social support as normative samples.

Optimism

The way in which an individual perceives positive (optimism) or negative (pessimism) experiences to predict future outcomes, was measured and used to determine the level of optimism, as well as the impact of this variable on the QoL of participants in the study (Moyer et al., 2008). The Life Orientation Test (LOT) is a measure that is used to determine individual differences in levels of optimism and pessimism (Scheier & Carver, 1985). The LOT is a 12-item measure that contains eight scoreable statements along with four filler items, that generates an overall optimism score. Four of the items contain an optimistic outlook and four items portray a pessimistic outlook, with the latter four items requiring reverse scoring. Thus, agreement for the optimistic items and disagreement for the pessimistic items are keyed positively. Each item is rated on a 5-point Likert scale ranging from 0 (strongly agree) to 4 (strongly disagree), with a theoretical total score ranging from 0-32. Higher scores indicate greater optimism. An example of an item that reflects optimism is, "In uncertain times I usually expect the best." A pessimistically portrayed item is, "Things never work out the way I want them to."

Data Analyses

Data analyses will be performed in two stages, preliminary and primary analysis. During the preliminary analyses, demographic information and descriptive statistics for participants and measures were investigated. Composite variables were also created for Physical and Emotional functioning in order to reduce the number of variables and attempt to improve the strength of the statistical analyses. Correlations among each set of

variables were conducted and z-scores were created for each measure in order for them to be combined to create a total standardized score representing the composite variable.

Analyses of the demographics of the participants at baseline were conducted to describe the participants in the study. Analyses were also carried out to determine if there were any differences between the 11 participants who were able to be contacted following the conclusion of the original QoL study and the remaining participants who participated in the original QoL study. Demographic variables such as age, gender, education, and duration of disease were explored to investigate differences between the two groups. The measures for the 11 current participants were examined to ensure the reliability was still in the acceptable range and to determine if there were any differences at baseline between this sample and the other sample of 16 individuals who did not participate.

Primary analyses were conducted in order to answer the two main research questions of this study.

Question 1a. Among the participants in this longitudinal study, can patients be divided into two distinct groups of those who can be characterized as doing better and worse in terms of Physical functioning, Emotional functioning, Social functioning, and Optimism at the current assessment? In order to determine who falls into the groups of doing better and worse, a median split analysis was conducted for each of the three domains (Physical, Emotional, and Social functioning) at each of the time points. Specifically, a pooled median value was computed at each time point for each of the domains and then a new dichotomous variable was created, indicating which participants

fall above the pooled median and which participants fall below, using the composite variables. Therefore, two groups will be created, those participants who fall above the median split and those participants who fall below. Ultimately, the median split technique will be the guideline to determine which participants seem to be doing better or worse.

Question 1b. If there are two groups, how does each group compare with the original sample that began the study in 1995, based on demographic variables and Physical, Emotional, Social functioning and Optimism at baseline? Once the group membership is established, each group will be compared to the original sample on demographic variables as well as the composite variables for each of the four domains.

Question 2. What aspects of QoL (Physical, Emotional, Social functioning), and Optimism at baseline, are most predictive of those participants who are doing better and worse at the most recent time point? Once the group of 11 participants are divided into the two groups of those doing better and worse at the most recent time point, a binary logistic regression will be conducted in order to determine which QoL variables at baseline predict group membership at the most recent time point.

Binary logistic regression is a variation of ordinary regression, which is used when the dependent variable is dichotomous, as in this case (i.e., doing better versus doing worse). The independent variables can be continuous, categorical, or both. Logistic regression forms a predictor variable and transforms the values of the predictor variable into probabilities of likelihood. In this way, logistic regression estimates the odds of a certain event occurring. Specifically, logistic regression produces odds ratios associated

with each predictor value, describing the probability of the outcome event occurring (i.e., the likelihood that a participant falls into the "doing better" or "doing worse" category).

Due to the small sample size in this study, both the significance test and effect sizes will be reported, in addition to the odds ratio. Binary logistic regression will be used to predict the dependent variable (doing better or worse) on the basis of the various independent variables (Physical, Emotional, Social functioning, and Optimism). Additionally, the percent of variance in the dependent variable that is explained by the independent variables will also be reported. The exact impact of the predictor variables will be explained using odds ratios. Therefore, this study will be able to determine which QoL variables at baseline significantly predict whether a participant is doing better or worse at the most recent time point.

Summary

Chapter Three described the methodology used in the present study. Descriptions of the participants, procedure, QoL measures, and data analyses were provided. Preliminary and primary analyses were subsequently conducted in order to answer the two main research questions of this 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 followed by the results of the primary analyses related to the research questions. All preliminary and primary statistical analyses were performed using the Statistical Package for the Social Sciences version 11.5 for Windows (SPSS 11.5). All statistical analyses used two-tailed tests of significance with an alpha level that was set at $p < .10$, which was established in order to compensate for the small sample size.

Participants in the current study represented two treatment groups. Those in the original transplant group (n = 3) received the fetal tissue transplantation surgery during the Parent Study, which has been described in the preceding chapters (Freed et al., 2001). Those in the optional transplant group (n = 8) received the sham surgery initially, and then subsequently received the fetal tissue transplantation procedure as part of the Parent Study (Freed et al., 2001). In the current study, statistical analyses compared the QoL of participants at the baseline, one-year, two-year, and the most recent assessment. Because the two treatment groups had surgery at least one year apart, adjustments were performed to align all the time periods following the transplantation surgery. In other words, baseline data for those in the original 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, their baseline data before the transplantation surgery 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 relative time since surgery instead of actual calendar time, the data from the two original groups were able to be combined and analyzed in terms of baseline, one year after surgery, two years after surgery, and the most current assessment. The following preliminary and primary analyses were based on the "shifted time" variables that were created by combining both groups into one group.

Preliminary Analyses

This section is organized in the following way: a) participant response to recent assessment request; b) demographic information; c) descriptive statistics of the QoL measures; d) reliability of variables used to analyze the research questions; e) correlations of QoL variables; f) explanation of the creation of composite variables.

Participant Response to Current Assessment

Participants from the original QoL study were contacted in the summer of 2008 to determine if they would be interested in being involved in a follow-up 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 participants who answered questionnaires that measured QoL. The questionnaires included the three original dimensions of QoL: Physical functioning, Emotional functioning, Social functioning, plus Optimism. The Physical functioning dimension of QoL was assessed 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 using the Center for Epidemiological Studies-Depression Scale (CESD), the State-Trait Anxiety Inventory-State Scale (STAI), the Parkinson's Disease Stress Scale, and the Intrusiveness of Illness Scale. The Social functioning dimension of QoL was assessed using the Social Provisions Scale (SPS). Finally, the Optimism domain was assessed using the Life Orientation Test (LOT). There was very little missing data in the questionnaires.

Demographic Information

A demographic questionnaire (Appendix K) was used to collect information on the participants' demographic characteristics at the most recent assessment period. These data are presented in Table 1, along with the data from the original QoL study with the current participants removed. As previously discussed in Chapter Three, this study was based on participants with PD who received fetal tissue transplantation surgery over 10-12 years earlier. Participants in the current study represent those who received the fetal tissue transplantation procedure initially during the Parent Study (n = 3; Freed et al., 2001), and those who initially received the sham surgery and later the fetal tissue transplantation (n = 8).

For the purpose of the present study, the demographic data is presented for the total sample of 11 individuals who participated in the most current iteration of data collection and then compared to those in the original QoL study. The 11 current participants were removed from the original QoL sample for comparison purposes ()n = 19). One-sample t-test revealed a significant difference in age between the participants in the current study when compared to those in the original QoL study. Specifically, those individuals in the current study were significantly younger than the original QoL sample ($t(18) = 4.442$, $p < .01$).

Table 1

Comparison of Demographic Information Between Current and Original QoL Study

Demographic Variables	**Current Study** (N = 11)	**Original QoL Study** (N = 19)
Gender:		
Male	3 (27.3%)	12 (63.2%)
Female	8 (72.7%)	7 (36.8%)
Age (baseline):		
Mean years	51.91 ± 7.53	61.11 ± 9.02**
Range	40-62	43-75
Duration of Disease (baseline):		
Mean years	13.64 ± 4.95	13.53 ± 5.37
Range	8-25	7-28
Ethnicity:		
Native American	0	1 (5.3%)
African American	0	1 (5.3%)
Caucasian	11 (100%)	15 (78.9%)
Hispanic	0	0
Asian	0	1 (5.3%)
Duration of Education (baseline):		
Mean years	16.82 ± 2.27	16.17 ± 2.55
Range	13-19	12-19
Current Living Situation (current assessment):		
Living with family	9 (81.8%)	13 (68.4%)
Living with friend or roommate	0	1 (5.3%)
Living alone	1 (9.1%)	4 (21.1%)
Living in residential setting	1 (9.1%)	0
Marital Status (currently assessment):		
Never been married	0	1 (5.3%)
Married or living with partner	9 (81.8%)	11 (57.9%)
Separated or divorced	1 (9.1%)	3 (15.8%)
Widowed	1 (9.1%)	3 (15.8%)
Current Paid Employment (current assessment):		
No	7 (63.6%)	13 (68.4%)
Part-time	3 (27.3%)	3 (15.8%)
Full-time	1 (9.1%)	2 (10.5%)
Volunteer work (current assessment):		
No	3 (27.3%)	14 (73.7%)
Yes	6 (54.5%)	1 (5.3%)
Previously, but not currently	2 (18.2%)	3 (15.8%)

** $p < .01$ level, two tailed.

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. The analyses included the number of respondents, means, and standard deviations (see Table 2). The presentation of each QoL dimension and Optimism includes baseline and the most recent assessment.

Table 2

Descriptive Statistics for QoL Measures and Optimism at Baseline and Most Current Assessment

	N	Mean	SD	Range (in this sample)
PHYSICAL FUNCTIONING (Lower Scores = Better Functioning)				
Activities of Daily Living (at worst)				
Baseline	11	27.36	6.67	13-37
Current	11	26.27	6.94	11-34
Severity of Symptoms (at worst)				
Baseline	11	12.09	2.67	7-15
Current	11	13.72	3.38	8-18
Free or Restricted Scale				
Baseline	11	3.91	1.64	2-6
Current	11	4.05	1.74	2-7
Physical Functioning Composite Variable (z-score)				
Baseline	11	.0000	.787	-1.74-1.07
Current	11	.1781	1.01	-1.72-1.70
EMOTIONAL FUNCTIONING (Lower Scores = Better Functioning)				
Center for Epidemiological Studies Depression Scale				
Baseline	11	30.91	9.24	20-46
Current	10	32.90	7.81	22-49
State-Trait Anxiety Inventory				
Baseline	11	30.73	9.54	20-49
Current	11	39.36	6.98	28-48
Intrusiveness of Illness Scale				
Baseline	11	61.64	19.02	23-85
Current	10	59.10	22.54	29-90
Parkinson's Disease Stress Scale				
Baseline	11	6.18	3.49	0-12
Current	11	8.59	3.09	2-13
Emotional Functioning Composite Variable (z-score)				
Baseline	11	.0000	.792	-1.26-1.33
Current	10	.3445	.742	-.74-1.76

Table 2, continued

Descriptive Statistics for QoL and Optimism Measures at Baseline and Most Current Assessment

	N	Mean	SD	Range (in this sample)
SOCIAL FUNCTIONING (Higher Scores = Better Functioning)				
Social Provisions Scale				
Baseline	11	85.18	9.00	69-94
Current	11	73.18	11.43	58-96
OPTIMISM (Higher Scores = Better Functioning)				
Life Orientation Test				
Baseline	11	21.27	4.36	15-30
Current	11	21.45	3.98	16-28

Reliability of Measures

Estimates of reliability (Cronbach's alpha) of the QoL measures for the most recent assessment were conducted as part of the preliminary analyses and as a measure of internal consistency (see Table 3). Because the Free or Restricted variable of the UPDRS is a single item, a reliability coefficient was unable to be calculated. Although the Severity of Symptoms at Worst had a somewhat lower reliability value (.68), it was included in the analyses because it is still in the acceptable range and has been consistently used in previous work with these data. Altogether, reliability estimates appear to be acceptable for all measures (Heppner, Wampold, & Kivlighan, 2008).

Table 3

Reliability of QoL Measures for Current Assessment

QoL Measures at Current Assessment	Cronbach's Alpha
Physical Functioning	
Activities of Daily Living at Worst Scale	.88
Severity of Symptoms at Worst Scale	.68
Emotional Functioning	
Center for Epidemiological Studies-Depression Scale	.84
Intrusiveness of Illness Scale	.94
State-Trait Anxiety Inventory-State Scale	.86
Social Functioning	
Social Provisions Scale	.95
Optimism	
Life Orientation Test	.78

Correlations of Quality of Life Variables

Correlations of the measures comprising the Physical, Emotional, and Social dimensions of QoL were calculated to describe the strength and direction of the linear relationship between the variables. Additionally, the assumptions of normality, linearity, and homoscedasticity were tested.

First, the Physical 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 variables for Activities of Daily Living at Worst Scale, Severity of Symptoms at Worst Scale, and the 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. Shapiro-Wilks statistics for test of normality revealed no violations of the assumption of normality for the three variables within the Physical functioning domain. 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. Therefore, 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 for all variables within the Physical functioning domain are presented in Table 4. Results indicated strong, positive

correlations among the measures, which justified putting them together to create the composite variable of Physical functioning.

Second, 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. 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 four variables indicated there was not a violation for the linearity and homoscedasticity assumptions. 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, and the Parkinson's Disease Stress Scale were investigated using a Pearson correlation coefficient. Correlation coefficients are presented in Table 5. Results indicated that two of the correlations were not strong (.14 and .08). However, because these four measures had been combined to create the composite variable of 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.

Finally, the Social functioning and Optimism domains of QoL were analyzed. As before, preliminary analyses were performed to determine whether there were any violations of the assumptions of normality, linearity, and homoscedasticity for the measures of the Social Provisions Scale and the Life Orientation Test. The scores on each variable appeared to be relatively normally distributed after viewing the histograms. Shapiro-Wilks statistics for the test of normality revealed no apparent violations of the assumption of normality for the measure of Social functioning or optimism. In addition, the normal probability plots indicated a normal distribution. Scatterplots for all variables indicated there was not a violation for the linearity and homoscedasticity assumptions.

Table 4

Pearson Correlation Coefficients for QoL Variables: Physical Functioning

	Activities of Daily Living at Worst	**Severity of Symptoms at Worst**	**Free or Restricted**
Activities of Daily Living at Worst			
Pearson Correlation	1		
Significance	N/A		
N	11		
Severity of Symptoms at Worst			
Pearson Correlation	.76**	1	
Significance	.007	N/A	
N	11	11	
Free or Restricted			
Pearson Correlation	.61*	.75**	1
Significance	.045	.008	N/A
N	11	11	11

° $p < .10$ level, two tailed. * $p < .05$ level, two tailed. ** $p < .01$ level, two tailed.

Table 5

Pearson Correlation Coefficients for QoL Variables: Emotional Functioning

	CESD	Intrusiveness of Illness	State-Trait Anxiety	Parkinson's Disease Stress Scale
Center for Epidemiological Studies-Depression Scale (CESD) Pearson Correlation Significance N	1 N/A 10			
Intrusiveness of Illness Pearson Correlation Significance N	.38 .280 10	1 N/A 10		
State-Trait Anxiety Inventory Pearson Correlation Significance N	.56° .089 10	.14 .695 10	1 N/A 11	
Parkinson's Disease Stress Scale Pearson Correlation Significance N	.73* .017 10	.68* .030 10	.08 .827 11	1 N/A 11

° $p < .10$ level, two tailed. * $p < .05$ level, two tailed. ** $p < .01$ level, two tailed.

Composite Variables

As previously discussed, several measures within the Physical and Emotional functioning domains displayed strong correlations with each other. Therefore, composite variables were created for Physical functioning and Emotional functioning. This was done in order to reduce the number of overall variables involved and in an attempt to improve the strength of the statistical analyses. Based on previous research conducted with these identical variables and the correlation among each set of variables, standardized 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 are included in Table 6.

Social functioning was assessed using the Social Provisions Scale and Optimism was assessed by using the Life Orientation Task. In order to address some of the following primary analyses, the two composite variables, Social Provisions Scale, and the Life Orientation Task were used.

Table 6

Reliability of Composite Variables for QoL Measures-Most Recent Data

	Cronbach's Alpha
Physical Functioning Composite Variable: Activities of Daily Living at Worst Severity of Symptoms at Worst Free or Restricted	.88
Emotional Functioning Composite Variable: Center for Epidemiological Studies-Depression Scale Intrusiveness of Illness Scale State-Trait Anxiety Inventory Parkinson's Disease Stress Scale	.74

Primary Analyses

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

Research Question 1

Question 1a. Among the participants in this longitudinal study, can patients be divided into two distinct groups of those who can be characterized as doing better and worse in terms of Physical functioning, Emotional functioning, Social functioning, and Optimism at the current assessment?

In order to determine who fell into the group of either doing better or doing worse at the most current assessment, a median split analysis was conducted for each of the three domains. The pooled median within each domain, and at each time point, was calculated and, then it was determined which participants fell above and below the pooled median value. Based on the valence within each of the domains, it was determined which individual participants appeared to be doing better and which individuals seemed to be doing worse than the entire group at the most recent assessment. Two groups of participants were identified based on whether or not they were considered doing "better" or "worse;" however, these groups were not consistent across the four domains and they were not entirely evenly distributed for all of the levels of functioning (See Table 7).

Table 7

Individual Participants Who Appear To Be Doing Better and Worse in Terms of Physical, Emotional, Social Functioning, and Optimism at Most Recent Assessment

	Better (Score)	**Worse (Score)**
Physical Functioning **Median = .2845** **Mean = .1781**	102 (-.11) 103* (-.44) 127 (-.11) 133 (-1.72) 134* (.28) 143* (-1.07)	105* (1.04) 114 (.41) 120 (1.70) 126 (.77) 137 (1.20)
Emotional Functioning **Median = .4029** **Mean = .3445**	103* (.35) 114 (-.69) 127 (.00) 133 (.07) 134* (.46) 143* (-.74)	102 (.84) 105* (1.76) 120 (.76) 126 (.63)
Social Functioning **Median = 72** **Mean = 73.18**	103* (73) 120 (89) 126 (73) 134* (78) 143* (96)	102 (72) 105* (58) 114 (72) 127 (71) 133 (62) 137 (61)
Optimism **Median = 22** **Mean = 21.45**	103* (24) 114 (27) 126 (23) 134* (28) 143* (23)	102 (17) 105* (19) 120 (22) 127 (21) 133 (17) 137 (16)

* Participants who were in Better or Worse group across all domains

There were three participants who were in the "better" group across all four domains and one participant who was a member of the "worse" group across all four domains.

Question 1b. If there are two groups, how does each group compare with the original sample that began the study in 1995 based on demographic variables and Physical, Emotional, and Social functioning, and Optimism at baseline? Once the group membership is established, each group will be compared to the original sample on demographic variables as well as the variables for each of the domains.

Although there were not two groups that were consistent in terms of the participants that fell in the "better" or "worse" group across all of the domains, there were two identifiable groups within each of the domains. Because a "better" and "worse" group could be identified for each of the four domains, those participants in each group were compared to the original sample in terms of demographic and relevant variables. When comparisons were made with the original sample, the participants in the current sample were removed from the original sample so as not to confound the results (see Table 8).

One-sample t-tests revealed significant differences between the participants in the "worse" group when compared to the original sample on two of the four domains. First, participants in the "worse" group at the most recent time point reported worse Physical functioning than participants in the original QoL Sample ($t(4) = -3.213$, $p < .05$). Second, in the Social functioning domain, participants who were in the "worse" group were found to have significantly less perceived social support than those participants in the original

sample $t(5) = -5.145$, $p < .01$). No significant differences were found on any of the domains between those participants in the "better" group and the original sample.

The three participants who were considered to be doing "better" across all four domains and the one participant who was consistently in the "worse" group across all four domains were compared to the original sample based on several demographic variables. Descriptive results showed that the three participants who were in the "better" group across all four domains were younger (difference was greater than one standard deviation) than the total original sample as well as the "worse" participants (see Table 9).

Table 8

Comparison of Means Between "Better" and "Worse" Group for Each Domain and the Original QoL Sample at Baseline

Domain	N	Mean	SD	t(df)	p
Physical Functioning (z scores)					
Current "Better" group	6	.2104	1.035	.575(5)	.590
Original QoL with "Better" removed	23	-.0323	.665		
Current "Worse" group	5	-.2525	.253	-3.213(4)	.032*
Original QoL with "Worse" removed	24	.1114	.809		
Emotional Functioning (z scores)					
Current "Better" group	6	.1155	.927	.157(5)	.881
Original QoL with "Better" removed	23	.0559	.891		
Current "Worse" group	4	-.1188	.774	-.361(3)	.742
Original QoL with "Worse" removed	25	.0210	.855		
Social Functioning					
Current "Better" group	5	81.60	9.450	.447(4)	.678
Original QoL with "Better" removed	24	79.71	9.526		
Current "Worse" group	6	66.00	6.356	-5.145(5)	.004**
Original QoL with "Worse" removed	23	79.35	8.912		
Optimism					
Current "Better" group	5	20.20	6.099	-.722(4)	.510
Original QoL with "Better" removed	24	22.17	5.569		
Current "Worse" group	6	22.17	2.483	.164(5)	.876
Original QoL with "Worse" removed	23	22.00	6.008		

^ $p < .10$ level, two tailed. * $p < .05$ level, two tailed. ** $p < .01$ level, two tailed

Table 9

Comparison of Demographic Variables for "Better" and "Worse" Groups and Original Sample

Demographic Variables	Original Sample with "Better" & "Worse" participants removed (N = 26)	"Better" Participants across all domains (N = 3)	"Worse" Participants across all domains (N = 1)
Gender			
Male	15 (55.6%)	---	---
Female	11 (44.4%)	3 (100%)	1 (100%)
Age (baseline)			
Mean years	59.04 ± 9.13	46.33 ± 3.51	56 ± ---
Range	40-75	43-50	---
Duration of Disease			
Mean years	13.93 ± 5.25	10.33 ± 2.52	10.00 ± ---
Range	7-28	8-13	---
Race			
Native American	1 (3.7%)	---	---
Black	1 (3.7%)	---	---
White	23 (85.2%)	3 (100%)	1 (100%)
Asian	1 (3.7%)	---	---
Duration of Education			
Mean years	16.38 ± 2.40	16.67 ± 3.22	14.00 ± ---
Range	12-19	13-19	---
Current Living			
Live w/family	20 (74.1%)	2 (66.7%)	---
Live w/roommate	1 (3.7%)	---	---
Live alone	4 (14.8%)	1 (33.3%)	---
Residential setting	1 (3.7%)	---	1 (100%)
Marital Status			
Never been married	1 (3.7%)	---	---
Married/cohabitating	19 (70.4%)	1 (33.3%)	1 (100%)
Separated/divorced	3 (11.1%)	1 (33.3%)	---
Widowed	3 (11.1%)	1 (33.3%)	---
Paid Employment			
No	19 (70.4%)	2 (66.7%)	1 (100%)
Part-time	3 (11.1%)	---	---
Full-time	3 (11.1%)	1 (33.3%)	---

Research Question 2

Question 2. What aspects of QoL (Physical, Emotional, Social functioning) and Optimism at baseline are most predictive of those participants who are doing better and worse at the most recent time point?

Relationships between each of the four predictor variables and the four outcome variables were calculated using Pearson correlation coefficients. The only relationship that approached significance was that between Social functioning at baseline and Physical functioning at the most current assessment ($r(11) = .739$, $p = .009$; see Table 10).

Four separate stepwise binary logistic regression analyses were conducted to assess the ability of Physical functioning, Emotional functioning, Social functioning, and Optimism, all at baseline, to predict whether or not participants were doing better or worse on the four domains at the most recent assessment. Regression analyses allow researchers to examine the relationship between variables, and determine if change in one predicts change in the other. Binary logistic regression analyses are used when the dependent variables are dichotomous (e.g., "better" or "worse"). For the binary analyses, the dependent variables were dummy coded as "better" or "worse" based on the median split technique, with the "better" group as the reference category, with the criterion for entry into the equation set at .10.

Due to the extremely small sample size in this study, there was a problem in the analyses that resulted from using logistic regression techniques. Specifically, because the 11 participants were further divided into two groups, there was not enough power to

determine if any of the variables at baseline were significant predictors of participant condition (e.g., "better" vs. "worse") on any of the variables at the most current assessment. Therefore, it was decided to use the dependent variables in their continuous form, subsequently increasing the power to be able to assess whether or not any of the independent variables at baseline were predictive of participants' Physical functioning, Emotional functioning, Social functioning, or level of Optimism over 10 years later.

Four multiple regression analyses were conducted in order to answer the question of whether or not the independent variables at baseline could predict QoL at the current assessment (Physical functioning, Emotional functioning, Social functioning and Optimism; see Table 11). The results of the regression analyses indicated that Social functioning at baseline was a significant predictor of Physical functioning at the most recent assessment ($R^2 = .714$, $F(4,6) = 3.742$, $p = .074$). There were no other significant results.

Table 10

Pearson Correlation Coefficients for Predictor and Outcome Variables

	Optimism-Current	**Social Support-Current**	**Physical Functioning Composite-Current**	**Emotional Functioning Composite-Current**
Optimism-Baseline				
Pearson Correlation	.113	-.390	.018	.210
Significance	.741	.235	.959	.560
N	11	11	11	10
Social Support-Baseline				
Pearson Correlation	.067	-.205	.739**	.318
Significance	.844	.546	.009	.370
N	11	11	11	10
Physical Functioning Composite-Baseline				
Pearson Correlation	.400	.434	.190	.173
Significance	.222	.182	.576	.632
N	11	11	11	10
Emotional Functioning Composite-Baseline				
Pearson Correlation	.100	.329	-.145	-.093
Significance	.769	.324	.670	.798
N	11	11	11	10

** $p < .01$ level, two tailed.

Table 11

Multiple Regression Analysis for Independent Variables at Baseline Predicting Dependent Variables at Current Assessment

Model	B	SE(B)	β	t	Sig.
Predicting Physical Functioning					
Optimism	-.088	.058	-.381	-1.512	.181
Social Support	.105	.029	.935	3.576	.012*
Physical Functioning	.269	.319	.209	.844	.431
Emotional Functioning	.092	.358	.072	.256	.806
R^2 = .714					
F = 3.742*					
Predicting Emotional Functioning					
Optimism	.011	.078	.067	.140	.894
Social Support	.022	.039	.284	.569	.594
Physical Functioning	.147	.427	.162	.344	.745
Emotional Functioning	-.003	.476	-.004	-.007	.994
R^2 = .133					
F = .192					
Predicting Social Support					
Optimism	-1.158	.968	-.442	-1.196	.277
Social Support	-.028	.487	-.022	-.057	.957
Physical Functioning	7.120	5.282	.490	1.348	.226
Emotional Functioning	-.254	5.938	-.018	-.043	.967
R^2 = .384					
F = .936					
Predicting Optimism					
Optimism	.039	.393	.043	.101	.923
Social Support	.018	.198	.041	.092	.930
Physical Functioning	2.045	2.142	.404	.955	.377
Emotional Functioning	-.107	2.408	-.021	-.044	.966
R^2 = .167					
F = .301					

* $p < .05$.

Summary

Chapter Four presented the results of the statistical analyses associated with the current study. The results of the preliminary analyses were discussed, followed by the results of the primary analyses utilized to address the research questions. Chapter Four was organized in the following manner: a) participant response to recent assessment; b) participants' demographic information; c) descriptive statistics related to the variables analyzed in the research hypotheses; d) reliability of variables analyzed in the research hypotheses; e) correlations of Physical and Emotional functioning variables; f) discussion of the creation of composite variables and g) results of statistic analyses.

It was initially proposed to run logistic regression analyses to explore whether or not QoL measures at baseline could predict if participants were doing better or worse in those domains over 10 years later. Unfortunately, due to the extremely small sample size, it was not possible for logistic regression to explore such hypotheses. Therefore, four multiple regression analyses were conducted to explore whether or not any of the independent variables at baseline were significantly predictive of participants' QoL at the current assessment. Results of the analyses revealed that Social functioning at the beginning of the study significantly predicted participants' physical functioning at the current assessment.

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) implications for future research, and e) conclusions.

Summary of the Study

There have been many improvements in the treatment of Parkinson's disease over time. Specifically, there has been a drastic advancement of surgical techniques for PD. Surgical procedures for PD are often considered when drug therapy is no longer effective. Different surgical procedures have been used over time to reduce symptoms of the disease. Fetal tissue transplantation surgery has been used as an experimental surgical treatment to improve PD symptoms since 1988 (Betchen & Kaplitt, 2003; Clarkson & Freed, 1999; Freed, Greene et al., 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) among individuals living with with PD.

This study examined the longitudinal effects on QoL among 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.), 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). Additional data were collected for at least two years after the blind was lifted.

In the present study, baseline data collected on QoL and Optimism from the original study were used as predictors of current status. The study specifically addressed the following research questions:

1. Can participants in this longitudinal study be divided into two distinct groups at the most recent assessment based on who can be characterized as doing better and

worse in terms of Physical, Emotional, and Social functioning as well as Optimism? If there are two groups, how does each of the groups compare to the original sample of participants who began the study in 1995 based on demographic variables and Physical functioning, Emotional functioning, Social functioning, and Optimism?

2. What aspects of QoL at baseline are most predictive of those participants who are doing better and worse at the most recent assessment?

Discussion of Overall Findings

The first research question was investigated to determine whether or not the 11 participants in this study could be divided into two groups at the most recent assessment, those who were doing "better" and those who were doing "worse," based on three aspects of QoL and a measure of optimism. The median for each of the four domains was found and participants were then placed into one of two groups: those falling above the median and those falling below the median. It was initially expected that there would be consistency across all of the domains. Specifically, those who were doing well in one domain were expected to be doing well in the other domains of QoL, and vice versa. Such consistency across domains was not found in this study. Participants were divided into "better" and "worse" groups for Physical functioning, Emotional functioning, Social functioning and Optimism; however, the group membership was not the same across the four categories.

Among all 11 participants, only three individuals fell into the "better" group for all four domains, and only one participant was consistently in the "worse" group. Thus,

the answer to the first research question is "no," participants cannot be divided into two distinct and consistent groups based on current QoL and Optimism scores. Results of this study suggest that the three specific aspects of QoL (Physical, Emotional, Social) and Optimism may be more independent of one another than was originally thought. Further research is needed to investigate how inter-related the aspects of QoL are in order to better understand what variables contribute to individuals doing better or not.

Following the exploration of whether or not participants in this study could be grouped into those doing "better" and "worse" on measures of QoL and Optimism, it was proposed that data from each of the two groups be compared with data of participants from the original QoL study. Specifically, t-tests were used to investigate whether or not there were differences in QoL and Optimism between the "better" and "worse" groups in each of the domains in the current study and the rest of the participants in the original study. All comparisons were calculated based on baseline data.

Results indicated that there were statistical differences between the participants who fell into the "worse" group in the domains of Physical and Social functioning, when compared with the participants in the original QoL study. Although the composition of the "worse" group was different for each of the domains, participants' scores in the "worse" group were significantly lower at baseline than scores of individuals who participated in the original study (with the scores of the "worse" participants removed).

The second research question was meant to investigate whether or not any of the three aspects of quality of life and/or the measure of optimism at baseline were predictive of participants doing "better" or "worse" at the most recently assessment. After learning

that two distinct and consistent groups could not be created across all four domains, it was determined that analyses would be conducted to separately explore predictors for each domain (e.g., Physical functioning, Emotional functioning, Social functioning, and Optimism). Logistic regression analyses are used to investigate independent variables as predictors of dichotomous dependent variables. Unfortunately, logistic regression analyses were insufficient in answering this question due to the extremely small sample size and the further division of the 11 participants into one of two groups ("better" vs. "worse") on each of the dependent variables (QoL and Optimism).

After determining that it was not possible to use logistic regression, four separate multiple regression analyses were conducted using the continuous forms of each dependent variable. Results of these analyses revealed that Social functioning at baseline was a significant predictor of Physical functioning at the most current assessment. Specifically, participants who had higher levels of perceived social support at the onset of the original QoL study reported better Physical functioning over ten years later. Although this was the only significant finding among the four regression analyses, the potential implications are very important. While the benefits of social support are often recognized in psychological research, it is less often included as an important variable within the medical field.

Limitations of the Study

Several limitations exist in the present study. First, the sample size is small because it was drawn from the population in the original Parent Study, which had a small sample size (N = 40) due to the nature of the surgical procedures involved. It was

originally determined that a sample size of 40 would be sufficient to show a treatment effect due to the fetal tissue transplantation surgery (Freed et al., 2001). Furthermore, the participants in this current study were drawn from the pool of 30 individuals who participated in the original QoL portion of the investigation (McRae et al., 2004). 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. Therefore, the total number of participants who were involved in the present study was quite small (n = 11). A further limitation related to the small number of participants in the current study, is the decision to set the significance level to .10 for all statistical analyses, which increases the likelihood that Type I error may have occurred.

This study lacks external validity due to the limited generalizability to a broad range of PD patients. This was a very unique study that involved experimental surgery and included the condition of sham brain surgery. It is likely that persons who volunteered for this study do not represent the general population of persons with PD because of their willingness to undergo such an experimental procedure.

Implications 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 a greater ability to investigate those participants who seem to be doing "better" versus those who are doing "worse," and explore predictors of participants' long-term condition with more accuracy and detail. 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 is fairly unlikely.

Because the individuals who volunteered for this investigation were unique in their choice to participate in such a study, the results of this study potentially have significant implications for the future treatment of PD and the understanding of what characteristics make patients good candidates for this particular treatment. There were three of the 11 participants in this study who consistently fell into the "better" group across all domains of QoL as well as Optimism. When exploring specific characteristics of these three individuals, it was noted that they were significantly younger than the original QoL sample. Therefore, age may serve as a moderating factor for long-term quality of life, as well as being a critical variable in deciding what individuals have the strongest chance at the best outcome following a surgical procedure such as this. However, it could also be that younger participants were more likely to participate in the present study, thus creating a biased sample based on ability and willingness to complete the questionnaires. Moderating effects were not assessed in this study due to the constraints of the small sample size and should be explored in future research.

Social support has been found to have health-related benefits and to buffer the physical and psychological effects of a wide range of stressors (Pennebaker & O'Heeron,

1984). A study that investigated the effects of social support on immune function among spouses of cancer patients found that individuals who were experiencing severe and chronic life stress showed evidence of better immunity if they had high levels of perceived social support (Baron, Cutrona, Hicklin, Russell, & Lubaroff, 1990). A very critical finding of the present study was the impact of Social functioning at baseline in predicting participants' Physical functioning so many years later. This result needs to be explored further in this study, but in other research as well. Additionally, further exploring differences between individuals at the onset of their participation in the study may be useful in better understanding characteristics that contribute to QoL over time.

Conclusions

The objective of the current study was to examine longitudinal predictors of QoL for people who received fetal tissue transplantation for PD over 10 years ago. This study is considered an important contribution to the research on PD and QoL due to the unique nature of the sample and the longitudinal aspect of the study.

The study found significant differences between groups at baseline and the most current assessment on measures of QoL such as Physical and Social functioning. The study also found Social functioning at baseline to be a significant predictor of Physical functioning over 10 years later. How and why some participants differed from others in terms of improvements and declines in functioning are questions to be explored further in future research.

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Appendix A

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)

	Normal	Adequate	Limited	Need Help	Unable To Do
Walking	_____	_____	_____	_____	_____
Dressing	_____	_____	_____	_____	_____
Cutting food	_____	_____	_____	_____	_____
Hygiene	_____	_____	_____	_____	_____
Getting up from chair	_____	_____	_____	_____	_____
Turning in bed	_____	_____	_____	_____	_____
Writing	_____	_____	_____	_____	_____
Talking	_____	_____	_____	_____	_____

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

	Normal	Adequate	Limited	Need Help	Unable To Do
Walking	_____	_____	_____	_____	_____
Dressing	_____	_____	_____	_____	_____
Cutting food	_____	_____	_____	_____	_____
Hygiene	_____	_____	_____	_____	_____
Getting up from chair	_____	_____	_____	_____	_____
Turning in bed	_____	_____	_____	_____	_____
Writing	_____	_____	_____	_____	_____
Talking	_____	_____	_____	_____	_____

Appendix B

Severity of Symptoms

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

	Normal	Mild	Moderate	Severe	Very Severe
Tremor	_____	_____	_____	_____	_____
Swallowing	_____	_____	_____	_____	_____
Salivation	_____	_____	_____	_____	_____
Freezing when walking	_____	_____	_____	_____	_____
Falling	_____	_____	_____	_____	_____

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

	Normal	Mild	Moderate	Severe	Very Severe
Tremor	_____	_____	_____	_____	_____
Swallowing	_____	_____	_____	_____	_____
Salivation	_____	_____	_____	_____	_____
Freezing when walking	_____	_____	_____	_____	_____
Falling	_____	_____	_____	_____	_____

Appendix C

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)

1	2	3	4	5	6	7
I still do everything I want to do						I can no longer do the things I want to do

Appendix D

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.

Yes	No	
____	____	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 D, continued

Parkinson's Disease Stress Scale

Yes	No	
____	____	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 E

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)

	Rarely	Some of the Time	Moderate Amount of Time	Most of the Time
1. I was bothered by things that usually don't bother me.	____	____	____	____
2. I did not feel like eating; my appetite was poor.	____	____	____	____
3. I felt that I could not shake off the blues even with help from my family or friends.	____	____	____	____
4. I felt that I was just as good as other people.	____	____	____	____
5. I had trouble keeping my mind on what I was doing.	____	____	____	____
6. I felt depressed.	____	____	____	____
7. I felt that everything I did was an effort.	____	____	____	____
8. I felt hopeful about the future.	____	____	____	____
9. I thought my life had been a failure.	____	____	____	____
10. I felt fearful.	____	____	____	____
11. My sleep was restless.	____	____	____	____
12. I was happy.	____	____	____	____
13. I talked less than usual.	____	____	____	____

Appendix E, continued

The Center for Epidemiologic Studies Scale (CESD)

	Rarely	Some of the Time	Moderate Amount of Time	Most of the Time
14. I felt lonely.	____	____	____	____
15. People were unfriendly.	____	____	____	____
16. I enjoyed life.	____	____	____	____
17. I had crying spells.	____	____	____	____
18. I felt sad.	____	____	____	____
19. I felt that people disliked me.	____	____	____	____
20. I could not get “going.”	____	____	____	____

Appendix F

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).

	Not At all	Somewhat	Moderately	Very Much
1. I feel calm.	_____	_____	_____	_____
2. I feel secure.	_____	_____	_____	_____
3. I am tense.	_____	_____	_____	_____
4. I am regretful.	_____	_____	_____	_____
5. I am at ease.	_____	_____	_____	_____
6. I feel upset.	_____	_____	_____	_____
7. I am worrying over possible misfortunes.	_____	_____	_____	_____
8. I feel rested.	_____	_____	_____	_____
9. I feel anxious.	_____	_____	_____	_____
10. I feel comfortable.	_____	_____	_____	_____
11. I feel self-confident.	_____	_____	_____	_____
12. I feel nervous.	_____	_____	_____	_____
13. I am jittery.	_____	_____	_____	_____
14. I feel “high-strung.”	_____	_____	_____	_____
15. I am relaxed.	_____	_____	_____	_____
16. I feel content.	_____	_____	_____	_____

Appendix F, continued

State-Trait Anxiety Inventory-State

	Not At all	Somewhat	Moderately	Very Much
17. I am worried.	_____	_____	_____	_____
18. I feel over-excited and "rattled."	_____	_____	_____	_____
19. I feel joyful.	_____	_____	_____	_____
20. I feel pleasant.	_____	_____	_____	_____

Appendix G

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.

My illness interferes with my…

	Very Little						A Great Deal
Body Image	1	2	3	4	5	6	7
Eating Habits	1	2	3	4	5	6	7
Ability to Work	1	2	3	4	5	6	7
Financial Security	1	2	3	4	5	6	7
Preferred Recreation/Leisure	1	2	3	4	5	6	7
Responsibility in the Family	1	2	3	4	5	6	7
Family Relationships	1	2	3	4	5	6	7
Marital Relationships	1	2	3	4	5	6	7
Sexual Relationships	1	2	3	4	5	6	7
Personal Relationships with Friends	1	2	3	4	5	6	7
Plans for the Future	1	2	3	4	5	6	7
Freedom to Choose Time Alone	1	2	3	4	5	6	7
Ability to Express My Personality	1	2	3	4	5	6	7
Sense of Independence	1	2	3	4	5	6	7
Self-Esteem	1	2	3	4	5	6	7

Appendix H

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).

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

Appendix H, continued

Social Provisions Scale (SPS)

	Strongly Disagree	Disagree	Agree	Strongly Agree
11. I have close relationships that provide me with a sense of emotional security and well-being.	_____	_____	_____	_____
12. There is someone I could talk to about important decisions in my life.	_____	_____	_____	_____
13. I have relationships where my competence and skill are recognized.	_____	_____	_____	_____
14. There is no one who shares my interests and concerns.	_____	_____	_____	_____
15. There is no one who really relies on me for their well-being.	_____	_____	_____	_____
16. There is a trustworthy person I could turn to for advice if I were having problems.	_____	_____	_____	_____
17. I feel a strong emotional bond with at least one other person.	_____	_____	_____	_____
18. There is no one I can depend on for aid if I really need it.	_____	_____	_____	_____
19. There is no one I feel comfortable talking about problems with.	_____	_____	_____	_____
20. There are people who admire my talents and abilities.	_____	_____	_____	_____
21. I lack a feeling of intimacy with another person.	_____	_____	_____	_____
22. There is no one who likes to do the things I do.	_____	_____	_____	_____

Appendix H, continued

Social Provisions Scale (SPS)

	Strongly Disagree	Disagree	Agree	Strongly Agree
23. There are people I can count on in an emergency.	_____	_____	_____	_____
24. No one needs me to care for them.	_____	_____	_____	_____

Appendix I

Life Orientation Test (LOT)

Indicate the extent to which you agree with each of the items below. Be as accurate and honest as you can. There are no right or wrong answers. *(check one for each item)*

1. In uncertain times, I usually expect the best.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

2. It's easy for me to relax.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

3. If something can go wrong for me, it will.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

4. I always look on the bright side of things.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

5. I'm always optimistic about my future.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

6. I enjoy my friends a lot.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

7. It's important for me to keep busy.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

8. I hardly ever expect things to go my way.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

9. Things never work out the way I want them to.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

10. I don't get upset too easily.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

11. I'm a believer in the idea that "every cloud has a silver lining."
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

12. I rarely count on good things happening to me.
____Strongly Agree ____Agree ____Neutral ____Disagree ____Strongly Disagree

Appendix J

Social Contact Scale

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

____Not at all
____Once in the past month
____2 or 3 times in the past month
____About once a week
____Several days a week
____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
____Once in the past month
____2 or 3 times in the past month
____About once a week
____Several days a week
____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
____Once in the past month
____2 or 3 times in the past month
____About once a week
____Several days a week
____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 K

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 K, 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