A Study of Fetal Tissue Implantation for the Treatment of Parkinson's Disease: Can Self-Efficacy and Social Support Predict Physical Functioning and Perceived Treatment?

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A STUDY OF FETAL TISSUE IMPLANTATION FOR THE TREATMENT OF PARKINSON’S DISEASE: CAN SELF-EFFICACY AND SOCIAL SUPPORT PREDICT PHYSICAL FUNCTIONING AND PERCEIVED TREATMENT?

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Abstract

Few studies have comprehensively explored the benefit of fetal tissue implantation in Parkinson’s disease (PD) patients. This type of investigation is necessary to better understand how and why some participants in a double-blind investigation of fetal tissue implantation for PD improved following the surgical procedure while others did not (Freed et al., 2001). Data for the present study were collected during a quality of life (QoL) study conducted by McRae et al. (2004) that sampled PD patients who participated in Freed et al.’s (2001) double-blind investigation of fetal tissue implantation. Several aspects of QoL were examined in McRae et al.’s (2004) study, including perceived social support and self-efficacy.

The literature on chronic disease management has consistently demonstrated the important role self-efficacy and social support have on the overall functioning of those living with chronic disease, specifically PD (Chenoweth, Gallager, Sheriff, Donoghue, & Stein-Parbury, 2008; Montgomery, Lieberman, Sing, & Fries, 1994; Schreurs, De Ridder, & Bensing, 2000; Simpson, Haines, Lekwuwa, Wardle, & Crawford, 2006). Additionally, literature on the placebo effect has suggested that higher levels of self-efficacy and perceived social support can enhance and sustain the placebo effect (Crow et al., 1999; Howard, 2008; Kaptchuk et al., 2008; Miller et al., 2009). The present study examined the predictive ability of perceived social support and self-efficacy in regard to physical functioning and perceived treatment in a sample of PD patients who received fetal tissue
implantation. The study uniquely contributed to the literature because it was the first to examine the role of self-efficacy and the interaction between self-efficacy and social support on physical functioning and perceived treatment within this participant sample.

Results indicated that self-efficacy was a significant predictor of physical functioning at 12-months post-fetal tissue implantation while social support was not found to be a significant predictor. Self-efficacy and social support were not significant predictors of patients’ physical functioning 24-months post-fetal tissue implantation or of patients’ perceived treatment group 12-months after the initial surgery. Future research studies might consider examining the longitudinal role of social support and self-efficacy on patient responsiveness to and benefit from surgical interventions for PD.
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Chapter One: Introduction

Description of Parkinson’s disease

Parkinson’s disease (PD) is a chronic and progressive neurological disease that produces numerous motor and non-motor symptoms in those living with the disease (Jankovic, 2007). This disease is the most common neurodegenerative disorder in the aging population (Prakash & Tan, 2010). Specifically, PD is prevalent in 1% of adults 60 years and older in industrialized countries, affecting more than six million people worldwide and more than one million individuals in the United States (Post et al., 2007; Prakash & Tan, 2010; Menza et al., 2009). The pathology of PD is explained by a loss of dopamine neurons in the substantia nigra, a part of the basal ganglia region of the brain (Jankovic, 2007). Symptoms differ in presentation and severity from patient to patient and similarly have a variable impact on the lives of those with PD.

Onset, Progression, and Symptoms of PD

The onset of PD typically occurs between the ages of 55 and 75 (Jankovic, 2007). Clinical studies have tracked the course of the disease and have determined that its progression is variable rather than linear. Postural instability and gait difficulty are two symptoms that predict a more rapid deterioration in the earlier stages of PD. These two symptoms are the strongest prognostic factors of impairment and disability (Jankovic, 2007; Post et al., 2007).
The four cardinal motor symptoms of PD are tremor at rest, rigidity, akinesia, and postural instability. Flexed posture and freezing, or motor blocks, are two other classic symptoms of PD (Jankovic, 2007). The most common non-motor features of PD include autonomic dysfunction, cognitive or neurobehavioral disorders, sensory abnormalities, and sleep abnormalities. Cognitive decline and dementia are the most common cognitive dysfunctions that occur in the PD population. Neuropsychiatric disorders, such as depression and anxiety, often are present in the PD population, particularly in those who suffer from dementia as well (Jankovic, 2007). In fact, depression has been estimated to be prevalent in around 50% of the PD population (Ravina et al., 2007). Depression in patients with PD is often related to other clinical domains such as quality of life, progression of physical symptoms, and ability to care for oneself (Schrag, 2006).

**Treatment of Parkinson’s disease**

While there is no cure for PD, the disease can be treated with various drug and surgical interventions, which assist in treating the symptoms and managing the disease. These interventions help to decrease the interference the disease has on PD patients’ lives. These interventions can contribute to maintaining the quality of life and level of functionality desired by patients and their families.

The standard drug treatment for PD is with Levodopa or L-dopa (Krack et al., 2003). L-dopa is a dopamine agonist that operates as a substitute for the loss of dopamine in the basal ganglia. Cotzias et al. (1967) first discovered this drug treatment in 1967 and it has since remained the primary drug intervention to decrease the severity of the motor symptoms in PD. While this treatment benefits PD patients, responsiveness to this drug often decreases within five to ten years (Clarkson, 2001). Additional disadvantages of the
L-dopa treatment stem from the “on” and “off” periods when patients experience fluctuations in the therapeutic benefit. Specifically, those with PD experience improvements in mobility during the “on” periods but then also experience the return of active motor symptoms during the “off” periods (Limousin et al., 1998). Current research is focused on improving the mechanism of the L-dopa treatment in order to prolong its therapeutic benefit (Goole & Amighi, 2009). To sum, this drug treatment has advantages to PD patients through the drug’s ability to decrease motor symptoms; however, the complications and disadvantages involved with L-dopa use, particularly the decrease in effectiveness over time, often lead patients to explore other treatments for the PD.

Surgical interventions are one type of alternative treatment that can be pursued by PD patients. Most surgical interventions for PD attempt to increase dopamine production in the brain through in vivo techniques (Clarkson, 2001). Gene therapy, deep brain stimulation, and neuronal implantation are examples of surgical interventions for PD.

Gene therapy is a surgical intervention that attempts to re-establish normal brain activity by introducing a new gene into the area of the brain that is diseased (Kaplitt et al., 2007). In PD patients, gene therapies have introduced new genes into the basal ganglia region of the brain with hope of ultimately modifying neurotransmitter levels (Fiandaca, Forsayeth, & Bankiewicz, 2008). To date, three studies with small sample sizes have implemented gene therapy and have demonstrated the practicality and safety of this procedure. Gene therapy was originally developed as a research tool, but currently researchers are exploring ways to develop it as a clinical treatment because of its potential to alter the course of chronic diseases, such as PD. Long-term follow-up studies have yet to demonstrate the efficacy and long-term effects of gene therapy and thus this
surgical intervention has not yet been widely used with PD patients (Fiandaca et al., 2008).

A second type of surgical intervention that has been developed in attempts to treat the motor symptoms of PD is deep brain stimulation (DBS); (Limousin et al, 1998). DBS is a procedure that implants electrodes into the subthalamic nucleus of the brain, which are then stimulated with high frequency waves. This stimulation functions to decrease the debilitating motor symptoms observed in PD patients (Limousin et al, 1998). Researchers have conducted numerous long-term follow-ups since Limousin et al. first developed DBS in 1998, and the results are encouraging. PD patients have demonstrated improvements in a variety of motor symptoms that have been sustained for more than five years (Krack et al., 2003). Due to these encouraging results of long-term follow-up studies, DBS is considered by many to be the surgical intervention of choice for PD patients (Krack et al., 2003).

The third type of surgical intervention is neural implantation. Specifically, fetal tissue implantation has been the primary form of neural implantation used in the treatment of PD. Fetal tissue implantation is a surgical intervention that introduces fetal tissue into the brain to regenerate neurons lost due to neurologic disease. The best results of fetal tissue implantation in PD patients have come from studies where dopaminergic neurons have been derived from human fetal ventral mesencephalon (Clarkson, 2001). Since Lindvall et al. first conducted fetal tissue implantations with PD patients in 1989, patients have demonstrated improvements in motor symptoms and reduced necessary doses of L-dopa (Clarkson, 2001). As reviewed by Clarkson and Freed (1999), a series of open label trials of fetal tissue implantation were conducted with small sample sizes
throughout the 1990s. These trials demonstrated improvements in motor functions and decreases in the necessary dosages of L-dopa (Clarkson & Freed, 1999). In a later review of these clinical trials of fetal tissue implantation in PD patients, Clarkson (2001) determined that about two-thirds of PD patients exhibit moderate improvements in motor function following this surgical intervention.

Freed et al. (2001) assessed the efficacy of fetal tissue implantation through the first double-blind trial. One half of the PD patients received fetal tissue implantation and the other received a sham surgery. The study examined changes in PD symptoms in the implant surgery group compared to the sham surgery group by controlling for placebo effect of the surgery (Freed et al., 2001). Freed et al. found that 65% of those in the implant group demonstrated increases in dopamine activity while those in the sham surgery group did not demonstrate these same improvements. Patients who were 60-years-old or younger exhibited a significant decrease in motor symptoms; however, older patients showed little to no improvement in motor symptoms (Freed et al., 2001). By the 12-month follow-up, 15% of those in the implant group developed dystonia or dyskinesia. While the study demonstrated variable efficacy of fetal tissue implantation on PD symptoms, these conclusions were important for future developments in surgical interventions of PD (Freed et al., 2001). This examination of neural implantation reported by Freed et al. (2001) served as the foundational study upon which the present investigation was based.

To summarize the treatments available for PD, gene therapy and DBS have demonstrated potential for the treatment of PD today and in the future. These two procedures were developed in response to variable successes demonstrated by past
attempts to treat PD through surgical interventions. The history of surgical interventions for PD includes lesioning procedures, such as thalamotomies and pallidotomies, as well as implantation of adrenal tissue into the brain. Gene therapy and DBS were still in their infancy when participants in the present study received fetal tissue implantation in the second half of the 1990s (Freed et al., 2001). While fetal tissue implantation was developed more than 20 years ago, many have argued that there are areas involved in neural implantation that deserve further development (Lindvall, Kokaia, & Martinez-Serrano, 2004). Specifically, the mechanisms through which this intervention is most effective along with an examination of which types of patients have demonstrated the most benefit from neural implantation are topics that should be explored (Lindvall et al., 2004). These explorations will assist in the development of future neuronal implantation interventions and will inform the overall treatment process of PD. Moreover, little is known about the effect or predictive ability of quality of life variables on the treatment outcome of procedures such as neural implantation in the PD population (McRae et al., 2004). Therefore, the focus of the present study will explore the role of quality of life variables on the physical functioning benefits observed in some PD patients following fetal tissue implantations conducted during the parent study. These quality of life variables and changes in physical functioning will also be explored in the context of the placebo effect given the double-blind methodological design of the parent study by Freed et al. (2001).

**Quality of Life**

Quality of life (QoL) is a comprehensive term used to describe a variety of domains of an individual’s life. Despite the range of drug and surgical treatments, QoL in
those living with PD is affected in a variety of arenas and dimensions due to fluctuating motor and non-motor symptoms, progression, and unpredictability of the disease (Reuther et al., 2007). Side effects of medications also contribute to the QoL for those with PD. Additionally, depression and anxiety commonly develop in those with PD and ultimately have negative effects on QoL (Jankovic, 2007). Some patients may find it harder to leave the house, feel embarrassed by the symptoms, and struggle with the inability to depend on being “on.” Whether considered independently or collectively, these changes in physical and emotional functioning can influence the social relationships and general social functioning of patients with PD. All of these domains, physical, emotional, and social functioning, have important implications on QoL. These three domains were the focus of examination in a QoL study conducted by McRae et al. (2004) which followed many of the PD patients who participated in the parent study (Freed et al., 2001). The QoL study was the source of data for the present study.

**Self-efficacy**

One aspect of QoL that was not examined in the original QoL study is self-efficacy. Research questions in the present study explored this variable and how it contributed to the beneficial treatment outcome observed in some PD patients following fetal tissue implantation. Self-efficacy has been examined by numerous studies in the health psychology literature, most of which have demonstrated the influential role self-efficacy plays in a variety of health related outcomes (Lorig, Mazonson, & Holman, 1993; Schwarzer & Fuchs, 1995). This construct has been explored in the context of adoption of health behaviors as well as in the management of chronic disease. Self-efficacy was first found to benefit the outcome of self-management activities in patients
with arthritis and now has been extended to a range of chronic diseases (Lorig et al., 1993; Lorig et al., 2001). Self-efficacy has been a focus in the literature because it is one of the few factors related to chronic disease management that is amenable to change. Therefore, interventions such as The Chronic Disease Self-Management Program of Stanford University’s School of Medicine have been developed to increase self-efficacy in the chronic disease population (Lorig et al., 2001). Stanford’s program has developed curriculums specific to patients with a range of chronic diseases such as HIV/AIDS, diabetes, chronic pain, and arthritis (Lorig et al., 2001). Results from these studies demonstrate multiple beneficial health outcomes as a result of increased self-management self-efficacy, such as decreased disability, fewer medical visits, and less fatigue, and they appear to be maintained over time (Lorig et al., 2001).

Few studies have examined the role of self-efficacy in the management of PD. However, existing evidence suggests that there are beneficial effects of high levels of self-efficacy on management of PD (Chenoweth et al., 2008; Peteet, 2002, as cited in Chenoweth, et al., 2008; Montgomery et al., 1994). This evidence justifies the examination of self-efficacy in the PD population, particularly throughout the implementation of a medical intervention such as fetal tissue implantation. A measure of self-efficacy was adapted by Lorig et al.’s (1993) previous work and was used by McRae et al. (2004) in the QoL study to assess PD patients’ self-efficacy related to the management of their disease and attending circumstances at baseline and during each follow-up assessment of the parent study.
Social Support

A second variable that was examined in the original QoL study and has been widely studied in the psychological and medical literature in a range of patient populations was social support. Along with self-efficacy, the research questions of the preset study explored how perceived social support is related to the beneficial treatment outcome observed in some PD patients following fetal tissue implantation. Social support has been found to have beneficial effects on the management of chronic disease, commitment to medical regimens, and response to physiological stress. In response to the positive health outcomes observed in other chronic disease populations, the role of social support has been examined in the PD population (Brod, Mendelsohn, & Roberts, 1998 as cited in Backer, 2000; Ehman, Beninger, & Gawel, 1990; Schreurs et al., 2000; Simpson et al., 2006). This research affirms that there are a variety of benefits that social support provides to the management of and coping with chronic diseases such as PD. In the original QoL study, McRae et al. (2004) assessed perceived social support with the Social Provisions Scale (Cutrona & Russell, 1987).

Despite the well-documented independent beneficial effects of social support and self-efficacy on health outcomes, few studies have examined the interrelationship of these two constructs on health outcomes in chronic disease patients. Those studies that have, found a positive relationship between self-management behaviors, social support, and self-efficacy (Kaşikçi & Alberto, 2007). Therefore, these variables appear to be interrelated and should be investigated collectively in chronic disease populations. The present study sought to further establish this relationship within the context of PD following a surgical intervention, which in this case was fetal tissue implantation.
Placebo Effect

In attempt to examine the efficacy of fetal tissue implantation, the parent study compared changes in PD symptoms between the implant surgery group and the sham or control surgery group (Freed et al., 2001). This design was used to control for the effects of perceived treatment or placebo responses on changes in PD symptoms following a surgical intervention. The placebo effect is a phenomenon that has been recognized and discussed for many years. Improvements in a variety of medical diseases have been associated with placebos, particularly following sham surgeries (Goetz et al., 2008; Birch, 2006).

The placebo effect has been found to operate through a variety of mechanisms, and two that have been explored are self-efficacy and social support. In a meta-analysis of numerous articles, Crow et al. (1999) examined the role of expectancies in the placebo effect. In the context of Crow et al.’s (1999) review, expectancies refer to the patient’s expected outcomes following a medical intervention. Similarly, patient-related self-efficacy expectancies exist, such as self-management self-efficacy or patients’ beliefs that they can perform particular skills to manage the effects of an intervention or of their disease (Crow et al., 1999). Crow et al. (1999) conceptualized the placebo effect within four main determinants (patient, provider, patient-provider interaction, and treatment/setting) and four primary mechanisms (expectancy, anxiety reduction, classical conditioning, and social support) that were thought to act on health outcomes (health status, self-report, and objective measures). Within the mechanism of expectancy, various forms of self-efficacy (process expectancy, positive and negative outcome expectancy, interaction self-efficacy, and self-management self-efficacy) have been related to the
placebo effect, how it operates, and how it produces responses (Crow et al., 1999). In theory, enhancements in self-efficacy will lead to increases in the placebo response, and within the health care field this increase in placebo response translates to improvements in health outcomes (Crow et al., 1999). This theory is supported by research that demonstrates enhancements in general health following increases in self-efficacy (Holman & Lorig, 1992; Schwarzer & Fuchs, 1995) and by literature that illustrates health benefits following from placebo responses to medical interventions (Birch, 2006). In their review, Crow et al. (1999) conclude that the literature indicates that increases in various forms of self-efficacy lead to enhancements in placebo responses. Similarly, social support has been found to be a mechanism through which the placebo response operates. Some studies have even demonstrated that the placebo effect is enhanced and sustained when supplemented with perceptions of social support (Kaptchuk et al., 2009). Therefore, these two QoL variables, self-efficacy and perceived social support, were examined as mechanisms of the placebo effect, based on patients’ perceived treatment, observed in PD patients following either an actual or a sham fetal tissue implantation surgery in the parent study.

**Statement of Purpose**

While numerous studies have been conducted to explore the efficacy of surgical interventions on the symptoms of PD, few studies have comprehensively explored the benefit of fetal tissue implantation. In particular, researchers have not identified the characteristics that make patients good candidates for this treatment with the exception of age, as discussed in Freed et al.’s (2001) investigation. In other words, researchers have not explored the variables that likely contribute to positive outcomes following the
procedure. Also, few studies have investigated the mechanisms through which potential benefits of fetal tissue implantation are likely to operate (Lindvall et al., 2004). As previously mentioned, this type of investigation is necessary to better understand how and why some PD patients improved following fetal tissue implantation in the parent study while others did not (Freed et al., 2001). Likewise, this sort of study will inform future surgical interventions with PD patients and assist in selecting candidates who might benefit the most from these surgeries. Additionally, this information can assist in determining domains of patient life that may require preliminary intervention or improvement prior to undergoing an invasive surgical procedure such as fetal tissue implantation. For example, interventions designed to improve patients’ level of self-management self-efficacy, such as Lorig’s (2001) Chronic Disease Self-Management Program, may be implemented prior to a surgical procedure in attempt to increase the potential benefit of surgery.

The present study attempted to address this gap in the literature by exploring the relationship of self-efficacy and social support on physical functioning in PD patients following fetal tissue implantation and at several follow-up assessments. Moreover, this study explored the relationship between self-efficacy, social support, and perception of treatment within this sample of PD patients who either received an actual fetal tissue implantation surgery or a sham surgery prior to the actual fetal tissue implantation. This investigation made a unique contribution to the literature by describing the role of self-efficacy and social support in physical functioning and perceived treatment observed in PD patients following fetal tissue implantation or sham surgery.
The literature on chronic disease management has consistently demonstrated the important role self-efficacy and social support have on the lives and overall functioning of those living with chronic disease. This research has extended specifically to patients living with PD and has illustrated that higher levels of perceived social support and self-management self-efficacy lead to more positive health outcomes within this population. Moreover, the literature has begun exploring the interrelationship between these two variables, self-efficacy and social support, within the chronic disease population (Chenoweth et al., 2008; Peteet, 2002 as cited in Chenoweth et al. 2008). While sparse, this growing research suggests that self-efficacy and perceived social support work collectively to benefit individuals managing chronic diseases (Kaşikçi & Alberto, 2007). The benefit of these variables would likely be of particular importance following medical interventions, such as surgery. Hence, the present study explored the relationship between these two constructs within the PD population following fetal tissue implantation.

Lastly, due to the unique design of the parent study, self-efficacy and social support were also explored as contributors to the placebo effect or as predictors of patients’ perceived treatment group (real or sham surgery). Literature on the placebo effect has suggested that higher levels of self-efficacy and perceived social support can enhance and sustain the placebo effect (Crow et al., 1999; Howard, 2008; Kaptchuk et al., 2008; Miller et al., 2009). This enhancement can lead to greater improvements in health outcomes such as physical functioning. Therefore, the present study sought to describe how these variables operate collectively and explored the effect this relationship may have on the physical functioning of PD patients following fetal tissue implantation.
Data for the present study were collected during the original QoL life study conducted by McRae et al. (2004). Thirty of the 40 patients who participated in Freed et al.’s (2001) parent study agreed to participate in the QoL study. Data on these QoL variables were collected at baseline, four-, eight-, 12-, 24-, and 36-month follow-up assessments. The present study examined the predictive ability of self-efficacy and perceived social support at baseline on physical functioning at 12- and 24-months post-fetal tissue implantation and perceived treatment of the patients 12-months after the initial surgery. Because patients who originally received the sham surgery were given the opportunity to have the actual fetal tissue implantation once the blind was lifted 13-months after the initial surgery, this study examined the patient data at 12- and 24-months after the actual fetal tissue implantation (or 24- and 36-months after the initial surgery for those in the sham surgery group).

**Research Questions**

1. Are self-efficacy and perceived social support at adjusted baseline correlated with physical functioning at 12- and 24-months post-fetal tissue implantation?

2a. Do self-efficacy and perceived social support at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation? Does the interaction term of social support x self-efficacy at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation?

2b. Do self-efficacy and perceived social support at adjusted baseline predict physical functioning 24-months following fetal tissue implantation? Does the interaction term of social support x self-efficacy at adjusted baseline predict physical functioning of PD patients 24-months following fetal tissue implantation?
3. Do self-efficacy and perceived social support at true baseline predict perceived treatment at 12-months after the initial surgery?

Summary

Chapter One provided an introduction of PD and the parent study upon which the present investigation was based. Specifically, a definition of the disease and its onset, symptoms, progression, and treatments were described. The impact of PD was discussed in terms of QoL implications and a brief overview of the various domains that comprise QoL in this study was presented. A summary of the present study was provided and accompanied by a rationalization for further study within the PD population following fetal tissue implantation. In Chapter Two, a more comprehensive review of the literature on PD, drug treatments, surgical treatments (specifically fetal tissue implantation), self-efficacy, perceived social support, and the placebo effect will be presented.
Chapter Two: Literature Review

Introduction

Chapter Two provides a review of relevant literature on PD and related treatment approaches. This chapter will examine the placebo effect, its determinants and influences, and its role in medical interventions, particularly in relation to those with PD. Self-efficacy will also be discussed in general as well as in the context of medical interventions and self-management of chronic disease. Next, social support will be explored as a general construct and then as a mechanism through which the placebo effect operates and ultimately effects health outcomes. Lastly, relationships between the domains of the placebo effect, self-efficacy, and social support will be explained.

The literature reviewed in this chapter was obtained through Internet searches in the following medical and psychological databases: PsychINFO, PsychArticles, MEDLINE, HealthFinder, and Academic Search Premier. The search terms used were Parkinson’s disease, levodopa, gene therapy, stem cell implantation, fetal tissue implantation, lesions, placebo effect, self-efficacy, self-management, self-care, quality of life, and social support. Books were also obtained from local university libraries that discussed the placebo effect, self-efficacy, and social support. Lastly, the reference lists from identified sources were reviewed to locate additional works or authors that were relevant to the present study.
**Parkinson’s disease**

Originally studied by and later named after James Parkinson, Parkinson’s disease (PD) is the most common neurodegenerative disease in the aging population (Prakash & Tan, 2010). PD is a progressive neurological disorder that affects a number of motor and non-motor features (Jankovic, 2007). These features differ in their severity and have a variable impact on the functioning of those who have been diagnosed with PD. The disease is diagnosed based on a set of clinical criteria and cannot be determined by a single test. In its early stages, PD symptoms can appear to be similar to those of other diseases, primarily essential tremor, multiple system atrophy with parkinsonism, and progressive supranuclear palsy (Prakash & Tan, 2010). The pathology of PD is characterized by a “loss of dopaminergic neurons in the substantia nigra pars compacta (SNC) and accumulation of α-synuclein (α-SYN) containing Lewy bodies and neuritis” (Cersosimo & Benarroch, 2012).

**Onset and progression.** The age of onset of PD is typically between 55 and 75 years old (Jankovic, 2007). Many studies have attempted to track the progression of PD and have concluded that the progression of the disease is variable rather than linear. This research suggests that the deterioration is more rapid in patients with postural instability and gait difficulty in the earlier phases of PD (Jankovic, 2007). Post, Merkus, de Haan, and Speelman (2007) found that advanced age, postural instability, and gait difficulty are the strongest prognostic factors for impairment and disability. Other studies have also suggested that early signs of cognitive impairment and severity of motor symptoms at baseline are strong predictors of advanced motor impairment and disability (as cited in Post et al., 2007).
**Prevalence.** PD affects more than six million people worldwide and more than one million individuals in the United States (Prakash & Tan, 2010; Menza et al., 2009). It is considered the most common neurodegenerative movement disorder worldwide and the second-most common in the U.S. (Prakash & Tan, 2010; Menza et al., 2009). The prevalence of PD in industrialized countries in adults 60 years and older is 1% (Post et al., 2007).

Recent public health research has examined the effects of race and ethnicity on the diagnosis of PD. One such study by Dahodwala et al. (2009) concluded that African Americans had a relative risk of .43 and Latinos had a relative risk of .74 for being diagnosed with PD in comparison to their White counterparts. Dahodwala et al. (2009) did not report a relative risk for Asian Americans or other racial minority groups. However, another study by Willis, Evanoff, Lian, Criswell, and Racette (2010) examined racial differences in the incidence and prevalence of PD and concluded that Whites have a “substantially higher prevalence and incidence of PD” compared to African or Asian Americans. The analyses of Dahodwala et al.’s (2009) study adjusted for several other demographic variables including age, sex, income, and healthcare utilization and determined that racial differences observed in the diagnosis of PD were not explained by any of these variables (Dahodwala et al., 2009). Instead, Dahodwala et al. (2009) speculated that the observed racial differences may be accounted for by biological differences, education, or beliefs about aging and urged that future research continue to explore the “complex biological and social determinants of these disparities” in order to improve the healthcare of those with PD.
**Symptoms.** There are four cardinal motor features of PD: tremor at rest, rigidity, akinesia or bradykinesia, and postural instability (Jankovic, 2007). Two other classic features of PD are flexed posture and freezing, otherwise referred to as motor blocks. Other secondary motor symptoms include hypomimia, dysarthria, dysphagia, and sialorrhoea (Jankovic, 2007). The non-motor features of PD include autonomic dysfunction, cognitive or neurobehavioral disorders, sensory abnormalities, and sleep abnormalities. Autonomic dysfunction in patients with PD can manifest as sweating, sphincter and erectile dysfunction, and orthostatic hypotension (Jankovic, 2007). Typical cognitive dysfunctions include some form of decline or dementia. Dementia in PD patients is often associated with neuropsychiatric disorders such as depression and anxiety (Jankovic, 2007). The prevalence of depression in the PD population has been estimated to be at 50% and is associated with many poor outcome variables, such as decline in quality of life, progression of physical symptoms, and inability to care for oneself (Ravina et al., 2007; Schrag, 2006). Olfactory dysfunction, depression, and rapid eye movement sleep behavior disorder are non-motor symptoms that are considered to be preclinical markers of PD. An assessment of these non-motor symptoms is thought to assist in identifying groups that are at risk for developing PD (Prakash & Tan, 2010).

**Treatment of Parkinson’s disease**

**Drug treatments.** Levodopa (L-dopa) is the standard drug treatment for PD (Krack et al., 2003). L-dopa is a dopamine agonist or pro-drug that substitutes for the loss of dopamine in the basal ganglia, which is related to the presence of PD symptoms (Goole & Amighi, 2009). Once administered, L-dopa is converted to dopamine and stored in corresponding neurons. This drug was first discovered by Cotzias et al. (1967)
and was a dramatic breakthrough in the treatment of PD at that time. The most common
drug treatment for PD combines L-dopa with the decarboxylase inhibitor, carbidopa
(Clarkson, 2001). This medication combination reduces the breakdown of L-dopa in the
intestines, ultimately increasing its bioavailability (Clarkson, 2001).

However, this drug treatment has been shown to lead to long-term motor
complications (Clarkson, 2001). Responsiveness to L-dopa has been shown to decrease
over time, often within five to 10 years. This decrease in responsiveness is related to
“progressive degeneration of nigral dopaminergic neurons” that results in a loss of
dopamine buffering and ultimately, dyskinesia in patients (Clarkson, 2001; Goole &
Amighi, 2009). Specifically, L-dopa exhibits fluctuations between “on” effects, when the
medication produces improvements in mobility, and “off” effects, when the medication is
not active and the motor symptoms of PD are present (Limousin et al., 1998). Even
during “on” periods, PD patients are often impaired by dyskinesia. Due to the decrease in
responsiveness over time and the progression of the disease, increased doses are often
necessary to prevent the mild decline in functioning that typically occurs during the first
few years of drug treatment (Goole & Amighi, 2009). Recent pharmaceutical research is
focused on slowing down and targeting the release of L-dopa in order to prolong its
therapeutic effect. Despite side effects and progressive decrease in responsiveness, L-
dopa still remains the most powerful, common, and standard drug treatment for PD
(Goole & Amighi, 2009).

**Surgical interventions.** Due to the various complications and disadvantages to
drug treatments such as L-dopa, several surgical interventions have been developed to
offer patients with PD additional treatment options. Two early ablative procedures that
upon investigation did not demonstrate the anticipated effects were thalamotomy and pallidotomy (Fox et al., 2011). Some surgical interventions have focused on ways to increase dopamine production in vivo (Clarkson, 2001). Examples of these interventions include gene therapy and neuronal implantation. Deep brain stimulation is currently the most common surgical intervention. Because gene therapy and deep brain stimulation were still in the early stages of development when the present study began, they are only briefly reviewed below. Further information can be obtained from a search of the medical literature on gene therapy and deep brain stimulation as they relate to PD.

**Gene therapy.** Gene therapy has received attention and interest from clinical researchers attempting to offer more than palliative care to PD patients (Fiandaca et al., 2008). Researchers have attempted to convert gene therapy, originally a research tool, into a medical option with the potential of altering the course of the disease (Fiandaca et al., 2008). To date, there are three “Phase 1 studies” implementing gene therapy that have been completed with human subjects in the United States. All of these studies are considered to be small safety studies with very small sample sizes totaling just 30 participants across all three studies. The results from these studies point to the efficacy of gene therapy, although consideration must be given to the potential effects of placebo as well as the lack of long-term follow-up data available at this time. Two of these studies targeted palliative treatment by modifying neurotransmitter levels in the basal ganglia. Kaplitt et al. (2007) modified these levels by introducing an adeno-associated viral (AAV2) vector containing glutamic acid decarboxylase (GAD) and Eberling et al. (2008) examined the introduction of an AAV2 vector containing human aromatic L-amino acid decarboxylase (hAADC). The third study by Gasmi et al. (2007) focused on modifying
the progression of the disease by delivering a glial-cell-line-derived neurotrophic factor (GDNF) homolog to the striatum. Most importantly, results from these studies indicate that the participants did not experience any treatment-related adverse side effects. Therefore, it can be concluded that the procedure of delivering AAV2 into the basal ganglia is relatively practical and safe (Fiandaca et al., 2008). Long-term follow-up studies will reveal the efficacy and safety of these gene therapies from a neurological perspective (Fiandaca et al., 2008).

**Deep brain stimulation.** Deep brain stimulation (DBS) is a surgical intervention that attempts to treat the disabling motor symptoms of PD (Limousin et al., 1998). This treatment was developed in response to moderate success that was observed in lesion procedures like thalamotomies and pallidotomies. DBS procedures have been found to produce results as effective as these lesioning procedures, but with fewer adverse side effects (Betchen & Kaplitt, 2003). Unilateral pallidotomies are still considered efficacious and clinically useful for the treatment of motor fluctuations and dyskinesia according to a recent review of PD treatments by Fox et al. (2011). Similarly, unilateral thalamotomies are considered to be efficacious and possibly useful as adjuncts to L-dopa therapies (Fox et al., 2011). Further review of these two procedures is not within the scope of the present study and therefore will not be discussed further. For additional information, including clinical implications of the use of pallidotomy and thalamotomy with PD patients, please consult the medical literature.

The DBS procedure involves implanting electrodes bilaterally into the subthalamic nucleus of the brain (Limousin et al., 1998). The electrodes are placed by stereotactic guidance through imaging and electrophysiologic testing. Once implanted,
the electrodes are stimulated through high frequency waves which then result in decreased motor disability. Limousin et al. (1998) conducted the first trials of DBS with PD patients in 1998. Results from this study revealed improved motor function in patients while off medications at a 12-month follow-up. Limousin et al.’s study also demonstrated improvements in dyskinesia in patients on medications and improvements in dystonia in patients off medications following DBS.

Krack et al. (2003) examined the long-term effects of bilateral stimulation of the subthalamic nucleus in 49 PD patients over the course of five years. This study concluded that patients exhibited marked improvements in motor function while off medications and in dyskinesia while on medications. Specifically, improvements in tremor, rigidity, akinesia, gait, and postural stability were sustained over five years (Krack et al., 2003). Speech was the only motor function that did not demonstrate improvement at the five-year follow-up assessment. Many other studies have demonstrated similar improvements at long-term follow-up of DBS (Rodriguez-Oroz et al., 2004; Visser-Vandewalle et al., 2005). To date, thousands of patients with advanced PD have now undergone DBS in facilities around the world (Antoniades, Carpenter, & Temel, 2012). Due to the encouraging results of long-term follow-up studies such as Krack et al.’s (2003), DBS is considered by many to be the surgical intervention of choice for PD patients.

Neural implantation. In addition to drug and surgical interventions, neural implantation has been another intervention that has been investigated with PD patients. Neural implantation involves replacing dopamine-producing neurons in the substantia nigra so that these cells will release dopamine properly and “show the molecular, morphological, and electrophysiological properties of substantia nigra” (Lindvall et al.,
Two types of neural implantation are stem cell implantation and fetal tissue implantation.

**Stem cell implantation surgery.** Stem cells, or “clone forming, self-renewing, pluripotent, progenitor cells,” are highly valuable sources of implantation material in a variety of clinical settings and in a variety of diseases (Rice, Halfpenny, & Scolding, 2003, p. 351). While it is a complex task to replace cells lost through disease processes in attempt to induce functional recovery, animal research has demonstrated that replacement of neurons and reconstruction of damaged neuronal circuitry is possible (Lindvall et al., 2004). Moreover, evidence suggests that symptom reduction can occur in diseased patients following cell replacement (Lindvall et al., 2004). Research on stem cell implantation has given priority to studies with neurological diseases due to the few available treatments and the devastating progression of these diseases (Rice et al., 2003).

While stem cell implantation exhibits high potential for the treatment of PD symptoms, there are many areas that deserve further development. Lindvall et al. (2004) argued that selection criteria for appropriate candidates for stem cell implantation needs to be developed in order to identify those who are likely to benefit the most. Specifically, patients whose primary pathology is focused on the deterioration of dopamine neurons are better candidates than those who have pathological changes in systems not related to dopamine (Lindvall et al., 2004). Next, advancements related to the “dose” and location of grafts must be made in order to improve their functional efficacy. Lastly, developments in stem cell implantation must be explored in order to decrease the chance of adverse effects such as the risk for teratomas and tumors (Lindvall et al., 2004).
**Fetal tissue implantation surgery.** A second form of neuronal implantation that has been used in the treatment of PD is fetal tissue implantation. The best results of fetal tissue implantation have come from studies where dopaminergic neurons have been derived from human fetal ventral mesencephalon (Clarkson, 2001). Lindvall et al. (1989) conducted the first study exploring human fetal tissue implantation with PD patients. Since then, implantation surgeries have generally demonstrated improvements in motor skills and lowered the required doses of L-dopa for some patients (Clarkson, 2001). Specifically, in his review of clinical studies using fetal tissue implantation, Clarkson (2001) determined that around two-thirds of patients demonstrate moderate improvement in motor function following surgery and, therefore, report improved quality of life. Nevertheless, these clinical studies have produced variable results due to the low survival of dopamine cells after implantation. Studies have suggested that as few as 5% of the dopamine cells survive implantation (Clarkson et al., 2001; Zawada et al., 1998). Researchers have concluded that the number of years since the onset of the disease does not predict the benefit of implantation as it relates to motor skills or L-dopa dose due to the fact that positive results have been observed in patients with differing years of onset, ranging from five to 15 years (Clarkson, 2001). Similarly, implantation benefit has been found to appear within the first six months following surgery and an increase in benefit may be observed for somewhere between two and six years (Clarkson, 2001; Yuan et al., 2010). However, there is no evidence suggesting when the benefit of implantation will reach optimal performance or what the trajectory of improvement or decline is.

In addition to some of the adverse side effects that have been shown to accompany fetal tissue implantation, such as dystonia and dyskinesia, there are also limitations in
terms of the ethical, political, and social issues and implications related to using the tissue from aborted fetuses (Yuan et al., 2010). A discussion of these issues is beyond the scope of the present study and therefore will not be explored here. Additional information related to these arguments can be found in the most recent literature on fetal tissue and stem cell implantation.

Results from the parent study. The National Institute of Health (NIH) has funded two double-blind clinical trials examining the effects of fetal tissue implantation in patients with PD (Clarkson, 2001). The goal of these studies was to demonstrate the benefit of fetal tissue implantation over controls and to explore which patients benefit the most from surgical intervention (Clarkson, 2001). The first of these two NIH funded studies was conducted by Freed et al. (2001), and is the parent study and participant sample used in the analyses of the present study. In this study, 40 patients with severe PD were selected to receive either an implant of human embryonic dopamine neurons or a sham surgery, with 20 patients in each group (Freed et al., 2001). The study followed a double-blind procedure that was maintained for 12 months. Specifically, mesencephalic tissue from four embryos was implanted bilaterally into the putamen of the 20 patients in the treatment group. Those patients in the control group received a sham surgery, during which holes were drilled into their skulls without penetrating the dura (Freed et al., 2001). At a 12-month follow-up, those patients who received the sham surgery had not improved. In 65% of the patients who received the actual fetal tissue implantation, positron emission tomography (PET) scans showed that there was an observable 20% increase of dopamine activity in the putamen. Additionally, implant recipients under 60 years old demonstrated a significant decrease in symptoms, particularly motor symptoms,
while older patients demonstrated little to no improvement 12 months after surgery. Unfortunately, dystonia and dyskinesia developed in 15% of the implant recipients at 12-month follow-up (Freed et al., 2001).

The second study by Olanow et al. (2003) examined the effects of fetal tissue implantation in 34 patients with advanced PD. The patients were followed for 24 months and the study was double-blind with a placebo control group (Olanow et al., 2003). Olanow et al. concluded that there was not a significant treatment effect or a significant difference between the treatment and control group on a variety of motor symptoms as measured by the Unified Parkinson’s Disease Rating Scale (UPDRS). Nevertheless, the study did demonstrate that patients with fewer motor symptoms at the start of the study received some benefit following the implantation (Olanow et al., 2003).

While the results from the parent study, Olanow et al. (2003), and others using fetal implantation have limitations, many authors argue that this is not reason to discontinue studies investigating the use of fetal tissue in PD patients (Betchen & Kaplitt, 2003; Fox et al., 2011). Suggestions have been made to develop a more targeted implantation as well as to determine the appropriate therapeutic window to increase dopamine levels without inducing dyskinesias (Betchen & Kaplitt, 2003).

Placebo Effect

The placebo effect is a phenomenon that has been studied in numerous scientific and clinical fields for many years (Price, Finniss, & Benedetti, 2008). It has been of particular interest and debate in the medical field due to the clinical implications of placebo trials and interventions. Generally, placebos have been defined as “agents or procedures aimed at pleasing the patient rather than exerting a specific effect” (Price et
Improvements associated with placebos have been demonstrated in multiple sclerosis, pain disorders, and many neurological disorders. However, these same placebo-associated improvements have been questioned in other non-neurological disorders such as obesity, asthma, nausea, and hypertension (Hróbjartsson & Gøtzsche, 2001). Since the placebo effect was first formally studied in 1799, researchers and technology have identified many of the neurobiological and psychological mechanisms that operate in the placebo phenomenon (Colloca & Benedetti, 2005; Price et al., 2008). The placebo response has typically been defined as the change that occurs in symptoms or conditions in patients following the administration of a placebo. A response of this kind can only be considered a true placebo response when it occurs in the context of an experimental design when the placebo condition is compared to an untreated baseline group otherwise referred to as the “natural history group” (Price et al., 2008, p. 567).

**Psychosocial and environmental determinants.** Efforts have also been made to examine the psychosocial and environmental context that surround the patient and how this context may affect the placebo response through influences on the “patient’s expectations, desires, and emotions” (Price et al., p. 567). These contextual factors include processes such as classical conditioning, verbal persuasion, past experiences with treatments, and behaviors exhibited by the patients’ healthcare providers and primary supports. Naturally these contextual factors vary depending on the conditions of the study or the clinical situation. Given the range and magnitude of these factors, influence on the placebo response itself is variable as well (Colloca & Benedetti, 2005). This variability can be seen in the range of placebo effect sizes observed among studies of pain treatments, an area that has examined the placebo effect extensively (Vase, Riley, &
Price, 2002). However, attempting to assess the magnitude of the placebo effect and, in particular, making conclusions about the proportion of patients that respond to placebos is a difficult task. Nevertheless, the fact that some patients respond to placebos and others do not is known (Price et al., 2008).

**Cognitive and emotional determinants.** Similar to the way psychosocial and environmental factors influence the presence and magnitude of the placebo response, cognitive and emotional factors have been found to contribute as well (Price, et al., 2008). These cognitive and emotional factors include expected symptom intensity, desired symptom change, emotional change, and memory distortions. To illustrate, patients may expect to achieve a certain level of pain relief from a treatment, and this expectation can ultimately influence the placebo response. Likewise, a memory of past pain experience, or more generally symptom intensity, can influence expectations of future pain experiences and indirectly affect the placebo response (Price et al., 2008). Related to expectations of symptom intensity is the desire for a specific change in symptom. Desire, or “the experiential dimension of wanting something to happen or wanting to avoid something happening,” is likely associated with the placebo phenomenon (Price et al., 2008, p. 572). One study by Vase et al. (2004) demonstrated an interaction between desire for pain reduction and expected pain intensity. Specifically, these two factors contributed to pain analgesia and this model accounted for 38% of the variance observed in the placebo response (Vase et al., 2004).

One last construct that can moderate the influence of these cognitive and emotional factors and ultimately the placebo response is somatic focusing (Price et al., 2008). Somatic focusing has been found to function as a source of feedback of the
placebo effect. In other words, when patients attend to signs of physical improvement, it is viewed as evidence of the effectiveness of the placebo treatment that further increases the magnitude of the placebo response over time (Geers, Helfer, Weiland, & Kosbab, 2006). Other psychological processes may mediate a placebo response that is more unconscious, such as classical conditioning. For example, patients may develop conditioned physiological responses to the presence of conditioned stimuli, such as a pill or syringe. To conclude, there are a variety of mechanisms and conditions that underlie and influence the placebo response (Price et al., 2008). The mechanisms of self-efficacy and social support in relation to the placebo response will be explored later in this chapter after providing a discussion of each of these constructs independently.

**Neurobiological influences.** Studies examining the change in brain activity that occur as a function of the placebo effect have found reductions in neural activity in areas that process experiences of anxiety and pain (Price, et al., 2008). These reductions have also been found to occur with increases in neural activity in brain areas that are associated with emotion regulation. Dopamine release is involved in these pathways along with opioid and serotonergic mechanisms in the brain (Goetz et al., 2008). Generally, this research indicates that placebo responses are produced through processes of reward and aversion in conjunction with the associated neural activity in the brain (Price et al., 2008).

**Placebo effect and surgical procedures.** Sham surgeries have been used to study the therapeutic benefits of a surgical intervention as well as to explore the placebo response (Birch, 2006). These sham surgeries have been conducted in clinical trials with a variety of medical patients. As aforementioned, the use of a placebo or sham surgery
was part of the design of the parent study, from which the current study is derived. These sham surgeries are known to be associated with strong placebo effects (Birch, 2006). There are many explanations for what factors contribute to the placebo response following sham surgeries. Birch (2006) discussed the following explanations in his review of the placebo effect in medical procedures: minimal expectation to provide evidence for the treatment’s efficacy, the physical discomfort from the surgery, the meaning associated with the surgery, and the effects attributed to the loss of blood during the procedure. Generally, all of these explanations suggest that there are biological changes and effects that occur during sham surgeries that must be considered in the interpretation of a placebo response (Birch, 2006). A more complete discussion of the biological effects associated with sham surgeries can be found in the medical literature, as it is outside the scope of the current study.

**Placebo effect and PD.** Placebo trials have been used to study many new therapies for PD and have become a standard component of these clinical trials (Goetz et al., 2008). As previously mentioned, the placebo response is associated with motivation, reward, and response to novel stimuli and therefore neural pathways associated with dopamine activation are involved. Because of the diminished supply of dopamine in the neural pathway of PD patients, placebo treatments have focused on this patient population (Goetz et al., 2008). The placebo response has been studied in both medical and surgical trials with PD patients, and its effects have been examined in a range of disease symptoms. In a review of 11 medical and surgical placebo trials with PD patients, Goetz et al. (2008) found that the overall placebo response rate was 16% with a range of 0% to 50% of patients. This review found that some of the lowest placebo response rates
occurred in clinical trials examining disease modification in patients who did not have a need for symptomatic treatment (Goetz et al., 2008). Improvements in motor fluctuations appear to occur most often in medication trials compared to other target symptoms in PD patients. Lastly, surgical interventions appear to demonstrate the highest placebo response rates, though they typically had smaller sample sizes (Goetz, et al., 2008). According to Goetz et al.’s (2008) review, a positive placebo response does not appear to be associated with age, gender, PD duration, or baseline Hoehn and Yahr stage (a scale used to measure disease stage in PD patients).

Improvements associated with placebo treatments have been documented in relation to many of the cardinal symptoms of PD, but placebo responses in dyskinesia have not been well-studied. Goetz and Laska et al. (2008) examined the effects of a drug trial of Sarizotan and placebo on dyskinesia. The overall findings of their study suggest that dyskinesias are affected by placebo treatments (Goetz, Laska, et al., 2008). These positive changes in dyskinesias were not associated with changes in other PD symptoms.

Another study by Mercado et al. (2006) examined the placebo response to deep brain stimulation in PD patients’ motor scores according to the Unified Parkinson’s Disease Rating Scale (UPDRS III). The results from this study suggest that expectation and placebo response were significant predictors of change in motor scores of PD patients (Mercado et al., 2006). Specifically, the authors concluded that the placebo was particularly effective on bradykinesia but was not found to significantly change scores in tremor or rigidity (Mercado et al., 2006). As newer treatments are developed and made available for PD patients, such as DBS, it can be expected that the placebo response will continue to be a phenomenon studied by clinical researchers.
Within the present study, the mechanisms by which the placebo effect operated were of importance. Because several psychosocial, environmental, cognitive, and emotional determinants have been found to influence the presence and magnitude of the placebo effect, the mechanisms of specific variables within each of these domains have been examined (Price et al., 2008). Two such variables within the social and cognitive domains that may be related to the placebo effect are self-efficacy and social support (Crow et al., 1999; Kaptchuck et al., 2008; Miller, Colloca, & Kaptchuck, 2009). These two constructs will be discussed independently in this chapter followed by a discussion on the relationships between each and the placebo effect.

**Self-efficacy**

**Definition of self-efficacy.** Albert Bandura (1997) has consistently defined perceived self-efficacy as “beliefs in one’s capabilities to organize and execute the courses of action required to produce given attainments” (p. 3). Perceived self-efficacy, henceforth referred to as self-efficacy, affects the courses of action individuals choose to follow, the effort they put forth, and the way they will persevere when confronted with obstacles (Bandura, 1997). Additionally, self-efficacy influences resilience to adversity, thought patterns, experience of stress, and level of accomplishment. Self-efficacy is an essential component of personal agency and therefore a major basis of action and human behavior (Bandura, 1997). Bandura (2012) explains that within this self-belief system “people’s beliefs in their capabilities vary across activity domains and situational conditions rather than manifest uniformly across tasks and contexts in the likeness of a general trait” (p. 13). This is unlike related concepts, such as self-esteem, self-confidence,
and locus of control, as these concepts exist as more general natures or traits (Maibach & Murphy, 1995).

**Self-efficacy and social cognitive theory.** Social cognitive theory describes a casual structure that addresses how people develop competencies and regulate actions (Bandura, 1986). This structure consists of a triadic reciprocal causation in which “human functioning is a product of the interplay of intrapersonal influences, the behavior individuals engage in, and the environmental forces that impinge upon them” (Bandura, 2012, p. 11). The presence of these intrapersonal influences suggests that individuals can exert intentional influences over their lives and events that take place. In other words, they are active agents in their lives. Self-efficacy is considered to be one of these intrapersonal constituents (Bandura, 1986). It is through different forms of agency that people exercise influence on their lives. When individuals influence the conditions that are in their direct control, this is referred to as personal agency. In many contexts, individuals do not have direct control over events that affect them (Bandura, 1997, 2000). They must influence others that have the knowledge, means, or resources to attain the desired outcome or exercise proxy agency. The last form of agency refers to collective agency when individuals work together, combining skills, knowledge, and resources to achieve a desired outcome. Individuals operating within a forum of collective agency may have diverse self-interests but can still work toward a common purpose (Bandura, 1997, 2000).

**Sources of self-efficacy.** Peoples’ beliefs in their capabilities are developed from four different sources: mastery experiences, social modeling, social persuasion, and physical and emotional states (Bandura, 1997). The first source of self-efficacy, mastery
experiences, comes from one’s practical experience of success or accomplishment. When individuals experience frequent failure, particularly early on in the learning process, self-efficacy often decreases in that specific domain. However, if successes come too easily and quick results are expected, one may become discouraged by the experience of failure (Bandura, 2012). Therefore in order to develop resilient self-efficacy, individuals must experience accomplishments in the face of obstacles with “perseverant effort” (Bandura, 2012, p. 13). Bandura (2012) explains that resilience is “built by learning how to manage failure so that it is informative rather than demoralizing” (p. 13). Mastery experiences are the most influential and important source of self-efficacy as they provide the most direct and authentic information about one’s capabilities to succeed (Bandura, 1997).

The second source of self-efficacy comes from social modeling or observation of others (Bandura, 2012). Observing others as they succeed in similar contexts can provide information to one’s own ability to successfully perform in the same context. During social modeling, it is important that those being observed share similar characteristics to those observing (Bandura, 1997). These observations serve as indicators to measure one’s own capabilities and ultimately estimate the likelihood of success. Social modeling is considered to be a weaker source of self-efficacy than direct experience, but nevertheless is a mode of influence (Bandura, 1997).

Social persuasion is the third source of influence on self-efficacy. Individuals can be persuaded by significant others that they possess the necessary capabilities to master a given task (Bandura, 1997). Persuasion can be particularly effective if individuals harbor self-doubts about their capabilities and can support perseverance when difficulties arise (Bandura, 2012).
The fourth source of self-efficacy relies on information from one’s physical and emotional states. These types of somatic indicators are of particular importance in domains involved with “physical accomplishments, health functioning, and coping with stressors” (Bandura, 1997, p. 106). Physiological indicators may come from experiences of autonomic arousal, fatigue, or pain, which are indicative of physical inefficacy. Similarly, mood states, such as anxiety or depression, can provide individuals with information from which to judge their personal efficacy (Bandura, 1997). Therefore, enhanced physical status, reduced levels of stress and negative emotionality, and correct interpretations of bodily states can positively influence one’s sense of self-efficacy in related domains (Bandura, 1997).

In developing a judgment about one’s capabilities in a given domain, integration of information from all four of these sources is required. The weight that each domain is given is dependent on the specific domain being assessed as well as each individual’s integration rules (Bandura, 1997). Various cognitive processes are involved in integrating all of this information in order to form the self-concept of efficacy. These self-appraisal skills are developed through the growth of self-reflective meta-cognitive skills that examine “the adequacy of one’s self-assessments” (Bandura, 1997, p. 115).

Mediating processes. The effects of self-efficacy are mediated through a variety of processes. Social cognitive theory specifies a theory of learning that works through four main processes: selective, motivational, cognitive, and affective (Bandura, 1997). These processes assist in explaining how self-efficacy beliefs produce their effects. Selection processes refer to the decisions that individuals make about which activities they choose to engage in, or choice behavior (Bandura, 1997). These decisions are
informed by one’s beliefs about his or her capabilities to perform that specific activity. In other words, one’s perceived self-efficacy. Often individuals avoid tasks that they perceive exceed their capabilities and seek out tasks that they are confident they can perform instead (Bandura, 1977, 1986). Motivational processes refer to the beliefs individuals form about perceived capabilities of what they can do, anticipation of outcomes, goal setting, and planning courses of action (Bandura & Cervone, 1983). Motivation is often stronger when individuals believe they can reach their goals. Similarly, those with high levels of self-efficacy often demonstrate more perseverance to overcome obstacles than those with lower levels (Bandura & Cervone, 1983). In regard to cognitive processes, self-efficacy can affect thought patterns that encourage or discourage performance in a certain activity. These cognitive processes can therefore affect the determination of goals or aspirations, the visualization of performance outcomes, and quality of analytical thinking (Bandura, 1995; Maibach & Murphy, 1995). Lastly, self-efficacy has been found to regulate emotional states. The beliefs individuals hold about their capabilities to cope with threatening or difficult situations can affect how much distress they experience (Bandura, 1995). For example, those with high levels of self-efficacy manage to lower stress and anxiety by engaging in behaviors that reduce the present threat in their environment. Contrarily, low levels of self-efficacy across multiple domains can lead to depression (Bandura, 1995). In summary, self-efficacy affects the behavior individuals choose to engage in, the effort and persistence they put forth in an activity, their thought patterns, and emotional states. The quality of psychosocial functioning is greatly impacted by self-efficacy (Bandura, 1986).
**Measurement of self-efficacy.** In many empirical studies, self-efficacy is often erroneously treated as a generalized trait. Bandura (1997) explains that one’s efficacy varies across domains of functioning, but also varies within certain aspects of a single domain. Therefore appropriate measurement of self-efficacy “relies on a good conceptual analysis of the relevant domain of functioning” (Bandura, 2006, p. 310). Bandura (2012) argues that self-efficacy should be measured on a unipolar scale, ranging from zero to some maximum level of belief. He argues for this unipolar scale as opposed to a bipolar scale with negative gradations since individuals cannot possess a level of self-efficacy that is less than completely ineffectual, or zero. Similarly, Bandura explains that attempting to measure a “neutral” level of self-efficacy is meaningless, and instead a midpoint on a unipolar scale should be referred to as a moderate level of self-efficacy. Bandura (2012) also recommends that the wording of self-efficacy items use “can do” as opposed to “will do.” The statement “will do” most accurately refers to one’s intention to perform a task, not one’s belief that they have the capabilities to perform that task (Bandura, 2012). Moreover, efficacy scales with multiple gradations are considered to be more sensitive and reliable than those with few response options (Pajares, Hartley, & Valiante, 2001).

For many years, Bandura (1977) also described three measurable dimensions of the concept of self-efficacy: magnitude, strength, and generality. The domain of magnitude refers to the perceived difficulty of adopting a behavior. Strength relates to the level of certainty one has in his or her ability to perform a specific activity. And lastly, generality reflects the degree to which efficacy beliefs are related to other behavioral domains as well as across time (Bandura, 1977).
Recently, Bandura (2012) discussed the common misconstrual of self-efficacy as specific tasks when researchers are intending to assess activity domains. For example, measuring self-efficacy in academic achievement requires the measurement of a large scope of performances within this activity domain, not just one specific task. Self-efficacy is then the total score of all the items used to assess the activity domain, in this case academic achievement, rather than a specific item (Bandura, 2012). Frequently, self-efficacy measures have been “mischaracterized” as “highly specific and narrow in scope,” which is a misunderstanding of how to measure the construct (Bandura, 2012, p. 17).

**Self-efficacy and health functioning.** A number of studies have examined the influential role of self-efficacy in a range of health-related behaviors. Specifically, self-efficacy has been explored in the context of health promotion behaviors, reduction of health risk behaviors, and self-management of chronic disease (Lorig, Mazonson, & Holman, 1993; Schwarzer & Fuchs, 1995). The health behaviors examined in the literature are comprehensive: condom use, smoking cessation, healthy dieting, exercise, and preventative health behaviors such as cancer screenings (Schwarzer & Fuchs, 1995). These studies have consistently demonstrated that perceived self-efficacy is an essential component in regulating the “adoption of health promoting behaviors and the elimination of health impairing behaviors” (Schwarzer & Fuchs, 1995, p. 281). Moreover, the literature illustrated that self-efficacy influences the process of behavior change at various stages across the decision-making, initiation, and maintenance processes (Schwarzer & Fuchs, 1995).
In relation to chronic disease, the literature has established that self-efficacy to carry out self-management activities greatly improves the beneficial outcome of these practices (Lorig et al., 2001). Like the literature on health promotion and risk reduction behaviors, self-efficacy has been examined in the context of many chronic diseases such as heart attack recovery, chronic obstructive pulmonary disease, diabetes, chronic arthritis, chronic pain, organ transplants, and breast cancer (as cited in Holman & Lorig, 1992). Many of these studies investigated perceived self-efficacy to perform activities related to self-management or self-care. For example, diet, exercise, and medication management are a few common domains of activities that comprise self-management of chronic disease. Given the unique nature of activities involved with self-management in each specific chronic disease, researchers have developed questionnaires of self-management self-efficacy that are tailored to their disease of interest. Self-efficacy has been given much attention because it is one of the few factors related to chronic disease management that is amenable to change. Therefore, interventions have been developed to increase self-efficacy in the chronic disease population. As Lorig et al. (1993, 2001), Weng, Dai, Huang, and Chiang (2010), Davis, Carrieri-Kohlma, Janson, Gold, and Stulbarg (2006), and several other researchers have asserted, and in line with Bandura’s (1997) theory of self-efficacy, individuals are more likely to effectively manage their chronic disease if they feel confident in their capacity to self-manage.

**Self-efficacy and self-management of PD.** Few studies have examined the role of self-efficacy in the management of PD. One such study by Chenoweth et al. (2008) examined the role of various factors, including self-efficacy, in self-management with a group of individuals with moderate to advanced stages of PD following an acute illness.
event. This study found that self-efficacy predicted better self-management in individuals with PD and also demonstrated that familial support was associated with higher levels of self-efficacy (Chenoweth et al., 2008). These findings are consistent with those of another study by Peteet (2002), which demonstrated that both formal and informal support can be found to enhance self-efficacy and self-management in individuals with PD (as cited in Chenoweth et al., 2008).

A similar study conducted by Montgomery et al. (1994) explored the benefits of a program designed to promote health and educate patients with PD. The program had a variety of objectives: “improve health confidence, provide information and support, improve physical function through exercise, and work with the physician to optimize medical treatment compliance” (Montgomery, et al., 1994, p. 429). A total of 290 PD patients, 140 in the treatment group and 150 in the control group, participated in this intervention that was delivered via post mail. Montgomery et al. (1994) found that the treatment group demonstrated increased levels of exercise, reduced side effects, decreased “off” times in their L-dopa treatment, decreased summary scores on an overall measure of PD symptoms, and reduced doctor visits, hospital stays, and overall sick days when compared to the control group. Furthermore, Montgomery et al. (1994) found that the treatment group exhibited improvements in overall quality of life and self-efficacy scores. Montgomery et al. (1994) interpreted the improvements observed in the treatment group to have occurred through the mechanisms of increased exercise and increased levels of self-efficacy.

While sparse, findings from these studies provide evidence for the beneficial effects of high levels of self-efficacy on management of PD. They further offer
justification for the examination of self-efficacy in this patient population, particularly throughout the implementation of a medical intervention.

Social Support

**Definition of social support.** Social support is an important construct that influences the placebo response, health outcomes, and levels of perceived self-efficacy (Chenoweth et al., 2008; Miller, Colloca, & Kaptchuck, 2009; Kaptchuck et al., 2008; Kaşikçi & Alberto, 2007; Penninx, Kriegsman, van Eijk, Boeke, & Deeg, 1996). Social support has been defined as “the perception or experience that one is loved and cared for by others, esteemed and valued, and part of a social network of mutual assistance and obligations” (Wills, 1991 as cited in Taylor, 2003). Social support is a concept that has been widely studied in the psychological and medical literature in a variety of patient populations. Social support can be provided in many different forms, such as informational support, instrumental support, and emotional support (Taylor, 2003; Uchino, 2004). These various forms of social support are typically examined in terms of coping with a particular stressor. Due to the broad range of benefits that have been associated with social support, it has been studied extensively.

Several theoretical models have been developed to conceptualize social support (Cutrona & Russell, 1987). Robert Weiss’s model of social provisions is one framework that has been considered by Cutrona and Russell (1987) to incorporate many of the major elements included across several conceptualizations of social support (as cited in Cutrona & Russell, 1987). Cutrona and Russell (1987) developed the Social Provisions Scale based on Weiss’s six functions of social relationships, and it is the measure that was used to assess social support in the present study. Weiss’s (1974, as cited in Cutrona &
Russell, 1987) model explains that relationships with others can serve six different provisions or functions. These six provisions are classified into two conceptual categories, “assistance-related” and “non-assistance-related” (Weiss, 1974, as cited in Cutrona & Russell, 1974). Within the assistance-related category, Weiss (1974, as cited in Cutrona & Russell, 1987) described the function of guidance, which typically comes in the form of advice or information from teachers or mentors, and reliable alliance, which is often provided by family members who can be depended upon for tangible assistance. In the non-assistance-related category, Weiss (1974, as cited in Cutrona & Russell, 1987) discussed the provisions of reassurance of worth, opportunity for nurturance, attachment, and social integration. Reassurance of worth is the recognition of one’s competence and value by others (Weiss, 1974, as cited in Cutrona & Russell, 1987). This kind of social provision can bolster one’s self-efficacy and ability to cope with stress more effectively (Cutrona & Russell, 1987). Weiss (1974, as cited in Cutrona & Russell, 1987) described the next social provision, opportunity for nurturance, as a sense that one is relied upon by others. While this provision cannot be considered social support, Cutrona and Russell (1987) discuss how this provision is an important aspect of interpersonal relationships that can enhance health and well-being. The fifth social provision is attachment, or the existence of a close relationship that provides emotional closeness and a sense of security. The sixth and final provision in Weiss’s (1974, as cited in Cutrona & Russell, 1987) model of social provisions is social integration which refers to a sense of belonging to a group of individuals who have a shared interest (Weiss, 1974, as cited in Cutrona & Russell, 1987). The positive affects of each of these social provisions may assist in promoting health and well-being (Cutrona & Russell, 1987).
Two different hypotheses have been developed to assist in describing how and under what circumstances social support operates. The first of these hypothesis is the “direct effects hypothesis”, which contends that social support is generally beneficial to both physical and psychological health during stressful and non-stressful times (Taylor, 2003). The second hypothesis is called the “buffering hypothesis” and argues that social support is keenly beneficial to overall health during stressful times but does affect health during non-stressful times. Specifically, the buffering hypothesis maintains that social support serves as a buffer to stress which ultimately allows an individual to handle stress more effectively (Taylor, 2003; Uchino, 2004). To date, research examining this concept has demonstrated evidence for both hypotheses and continues to support the conclusions from a classic work by Cohen and Wills (1985). Cohen and Wills (1985) have suggested that both conceptualizations of social support are evident, but the processes through which social support operates are different for each hypothesis. Specifically, the direct effect of social support is evident when measuring the level of integration into a social network. On the other hand, the buffering hypothesis is apparent when measuring the “perceived availability of interpersonal resources that are responsive to the needs elicited by stressful events” (Cohen & Wills, 1985, p. 310).

**Social support and health functioning.** In terms of psychological benefits, social support has been found to reduce depression and anxiety in times of stress (Lin, Ye, & Ensel, 1999). Moreover, social support has been found to enhance psychological adjustment to a variety of chronic diseases such as coronary artery disease (Holahan, Moos, Holahan, & Brennan, 1997), cancer (Penninx et al., 1998), and stroke (Robertson & Suinn, 1968). Social support has also been found to reduce cognitive decline in older
adults (Seeman, Lusignolo, Albert, & Berkman, 2001). Lastly, social integration has an impact on mortality, as those with higher levels of support have a lower risk of death (Seeman, 1996). In a hallmark study conducted by Spiegel, Bloom, Kraemer, and Gottheil (1989), individuals with metastatic breast cancer were found to have longer survival rates than controls after participating in supportive group therapy.

Interestingly, the use of one’s social support system is not necessary to reap its benefits. In fact, research has demonstrated that simply the perception of support can be stress-reducing and beneficial (Taylor, 2003; Thoits, 2011; Uchino, 2004). Penninx et al. (1996) performed a literature review on the effects of social support on chronic disease and concluded that the perception of social support is of greater importance than functional or structural support. Regardless of the type of chronic disease, positively perceived social support has been found to have favorable effects on the course of the disease (Barron, Cutrona, Hicklin, Russell, Lubaroff, 1990; Penninx et al., 1996; Uchino, 2004). Penninx et al. (1996) also concluded that the benefits of perceived social support extended to “psychological adjustment, well-being, functional status, and also more ‘objective’ health outcomes” (p. 223). In 1998, Penninx et al. examined the effects of social support, as measured by aspects of structural and functional support defined by the researchers, on coping with depressive symptoms in a group of participants with chronic diseases. Their study found that there were favorable effects of social support, particularly having a partner or close relationships, on depressive symptoms (Penninx et al., 1998). Similarly, Kahn, Hessling, and Russell (2003) explored the relationship between social support, negative affectivity, physical health, and well-being, specifically, depression symptoms, loneliness, and life satisfaction, in a sample of older adults. Their
study found that perceived social support, as measured by The Social Provisions Scale (Cutrona & Russell, 1987), was a strong predictor of well-being after controlling for negative affectivity (Kahn et al., 2003).

Social support has also been examined in the context of commitment to medical regimens. Specifically, Resnick, Orwig, Magaziner, and Wynne (2002) have suggested that adherence to an exercise program in a group of older adults was indirectly enhanced by the presence of social support, as measured by The Social Support for Exercise Habits Scale (Sallis et al., 1987) as it strengthened self-efficacy and outcome expectations. In summary, social support has been studied extensively and results consistently demonstrate a beneficial effect on chronic disease and health-promoting behaviors.

**Social support in PD.** In light of the demonstrated beneficial effects of perceived social support on chronic disease, this construct has been examined in patients with PD as well. The literature has consistently demonstrated that social support is related to positive health outcomes in PD patients (Brod, Mendelsohn, & Roberts, 1998; Ehman, Beninger, & Gawel, 1990; McRae et al., 2011). Studies have examined outcomes in terms of both physical and psychosocial health. A recent study by Simpson, Haines, Lekwuwa, Wardle, and Crawford (2006) examined the effects of social support on psychological functioning in 34 PD patients. Simpson et al. (2006) measured social support with a comprehensive approach by quantifying the presence of close relationships as well as examining the satisfaction with social support through the social support subscale of the Parkinson’s Disease Questionnaire (PDQ-39); (Jenkinson, Fitzpatrick, Peto, Greenhall, & Hyman, 1997). This study found that as levels of satisfaction with social support decreased, scores on depression, anxiety, and overall stress increased (Simpson, et al., 2006). Additionally,
this study revealed that positive affect was associated with quantitative measures of social support such as the total number of close relationships (Simpson et al., 2006). The relationships observed in this study were discussed in the context of clinical implications in psychotherapeutic treatment for PD patients.

Another study by Schreurs, De Ridder, and Bensing (2000) explored the role of coping and social support on quality of life in PD patients. Schreurs et al. (2000) measured received social support in their sample with the Social Support List (SSL-I) (Kempen & Van Eijk, 1995). The study concluded that passive coping styles were related to problems in the domains of physical, psychological, and social functioning (Schreurs et al., 2000). However, the adverse effects of passive coping did not extend to patients’ overall functioning at one-year follow-up. In opposition to their research hypothesis, Schreurs et al. (2000) did not find that quality of life was affected by patients’ attempts to seek support or the support they actually received. These results are in contrast with most other studies that demonstrate improved functioning and quality of life with greater social support (as cited in Schreurs et al., 2000). Schreurs et al. (2000) suggested that this finding may have resulted from a bias in their sampling method, as all of the patients studied were self-referred from a patient organization and, therefore, perhaps less likely to be isolated. In other words, these patients already had high levels of social support in their lives. The study did conclude that negative social interactions were associated with problems in psychological functioning (Schreurs et al., 2000).

A comprehensive study conducted by Backer (2000) examined illness-related stressors in 70 PD patients and the role of social support and coping style in physical and psychosocial health dysfunction. The illness-related stressors that were examined
included losses in functional abilities (difficulty getting out of bed and getting up from a chair, falls, inability to drive, etc.) as well as stressors incurred on a daily basis (depression, worry, medication side effects, etc.). In this study, social support was measured with the Medical Outcomes Study Social Support Survey (MOS-SSS) developed by Sherbourne and Stewart (1991). Backer (2000) concluded that greater dysfunction in psychosocial health was associated with low perceived availability of social support, frequent use of evasive coping, and more advanced stage of disease. Stage of disease was the only independent variable that was predictive of physical health dysfunction (Backer, 2000). Lastly, Backer’s (2000) study suggested that the four predictors examined (evasive coping, confrontational coping, perceived social support, and stage of disease) explained 31% of the variance in overall health dysfunction (psychosocial and physical health), 23% of the variance in physical health dysfunction, and 32% of the variance in psychosocial health dysfunction. The findings from this study provide implications for clinicians assessing overall health dysfunction in PD patients as well as those providing interventions to improve coping, availability of social support, and overall disease management (Backer, 2000).

The majority of findings from studies examining the role of social support in PD patients are consistent with the previously established literature, which documents the variety of benefits that social support provides to the management of and coping with chronic disease.

**Relationships Between the Placebo Effect, Self-efficacy, and Social Support**

*Placebo effect and self-efficacy.* In response to the established literature that discusses the independent roles of the placebo effect and self-efficacy on health
outcomes, researchers have explored the mechanism of self-efficacy, and more generally the theory of expectancy, on the placebo effect. Bandura (1977, 1986, 1997) described two forms of expectancy, outcome expectations and self-efficacy expectations, and these forms of expectancy have been used to explain the placebo effect (Stewart-Williams & Podd, 2004). A comprehensive meta-analysis by Crow et al. (1999) examined the mechanisms of several forms of expectancies on the placebo effect within medical literature and synthesized its findings from this research. The authors’ review conceptualized the placebo effect within a framework of determinants, mechanisms, and outcomes. Specifically, Crow et al. considered four main determinants (patient, provider, patient-provider interaction, and treatment and setting) and four primary mechanisms (expectancy, anxiety reduction, classical conditioning, and social support) that were thought to act on health outcomes (health status, self-report, and objective measures). The meta-analysis considered expectancy to be the most “inclusive” mechanism and, therefore, focused on this domain (Crow et al., 1999). Crow et al.’s review of 93 primary articles on this topic confirmed that expectancy is a mechanism through which placebos operate and produce responses. Specifically, they found that expectancies were accessed in three different clinical areas: preparation for medical procedures, management of illness, and medical treatment (Crow et al., 1999). Primary forms of expectancy that have been reviewed in the literature are process expectancy, positive and negative outcome expectancy, interaction self-efficacy, and self-management self-efficacy. As previously mentioned, the literature generally confirmed that various forms of self-efficacy led to beneficial health outcomes in all three clinical areas. As such, Crow et al. (1999) argued for the implementation of clinical interventions that seek to enhance these outcome
expectancies and various forms of self-efficacy to ultimately increase the well-documented benefits of the placebo response. A detailed review of each of the 93 primary articles will not be discussed here, but can be found in Crow et al. (1999).

In another discussion of the placebo effect and the related cognitive psychological processes, Howard (2008) utilized expectancy theory as one model to explain the mechanisms and effects of the placebo effect. Specifically, Howard (2008) stated, “the expectations or beliefs patients have about treatment will influence how they respond to treatment” (p. 16). By this notion, patients who have positive expectations about a treatment may experience beneficial outcomes, even if they are administered a placebo or sham intervention (Howard, 2008). Similarly, patients who have negative expectations about the outcome of a treatment may experience deleterious effects. These adverse effects to a placebo have been termed nocebo effects (Barsky, Saintfort, Rogers, & Borus, 2002). Howard (2008) also discussed the effect treatment providers’ expectations can have on the beliefs patients hold about the treatment and therefore contribute to a positive placebo or negative nocebo effect. Other theories have been used to explain the placebo effect, such as classical conditioning, but will not be discussed here, as they are not within the scope of the present study (Stewart-Williams & Podd, 2004).

Social support and the placebo effect. As mentioned in Crow et al.’s (1999) conceptual framework of the placebo effect, social support has been considered a mechanism through which the placebo effect functions. Researchers have investigated the role of social support on the placebo response in clinical trials (Kaptchuck et al., 2008; Miller, Colloca, & Kaptchuck, 2009). Most of this research has focused on the interaction and relationship between the patient and provider throughout the course of treatment.
Miller et al. (2009) explained that the placebo effect in the health care field relates specifically to the interaction between patients and clinicians, which leads to therapeutic outcomes such as symptom relief and coping with illness. One study by Kaptchuk et al. (2008) examined the role of the patient-clinician relationship in the placebo response in patients with irritable bowel syndrome who received a sham acupuncture treatment. The patients received the acupuncture from either a less supportive practitioner or a practitioner who demonstrated support and empathy. The results suggested that the placebo response was produced and it demonstrated therapeutic benefit by the sham acupuncture in this patient population (Kaptchuck et al., 2008). Furthermore, the study concluded that a larger percentage of participants who received the treatment by an acupuncturist who demonstrated support and empathy exhibited symptom relief than those who received the treatment from a less-supportive practitioner (Kaptchuck et al., 2008). In other words, the placebo was enhanced and sustained when supplemented by additional supportive communication during the acupuncture (Kaptchuk et al., 2008).

Miller et al. (2009) further discussed the various mechanisms through which the placebo response operates. Specifically, they discussed the placebo effect on a cultural level and explained that the placebo effect can be activated through the processes of social support (Miller et al., 2009). Similarly, Humphrey (2002) discussed the role of social influence and support on the placebo effect and explored the reasons why people often require “the intervention of others” or “outside permission” to take steps towards healing. Humphrey (2002) speculated that hope can activate internal healing processes and that this hope often comes from others. Miller et al. (2009) furthered this discussion and suggested “it is difficult to generate hope for relief by personal strategies,” but that
“it takes the intervention of an authoritative or protective figure to promote hope and expectation for relief, leading to the placebo effect” (p. 531). To summarize, social support has been found to be a mechanism through which the placebo effect operates in a variety of medical populations.

**Social support and self-efficacy.** Given the empirical evidence that demonstrates the independent beneficial effects of social support and self-efficacy on health outcomes, it seems likely that these two constructs simultaneously play a role in health outcomes, specifically in patients with chronic diseases like PD. As previously discussed in the context of social support, Weiss (1974, as cited in Cutrona & Russell, 1987) described “reassurance of worth” by others as one category of his model of social provisions. Cutrona and Russell (1987) conferred that the presence of this provision, or the recognition of one’s competence and value by others, may enhance one’s sense of self-efficacy and overall coping abilities. In other words, receiving this kind of positive feedback through supportive relationships can enhance one’s self-efficacy (Cutrona & Russell, 1987). Despite these conceptual links, few studies have examined the interrelationship of these two constructs, social support and self-efficacy, on health outcomes in chronic disease patients. One recent study by Kaşikçi and Alberto (2007) examined the role of familial support, perceived self-efficacy, and self-care behaviors in a sample of Turkish patients with chronic obstructive pulmonary disease. This study found positive relationships between self-care behaviors and familial support, self-care behaviors and self-efficacy, and familial support and self-efficacy (Kaşikçi & Alberto, 2007).
As previously discussed, self-efficacy has been found to predict self-management in PD patients (Chenoweth et al., 2008; Peteet, 2002 as cited in Chenoweth et al. 2008). Additional evidence for the relationship between social support, self-efficacy, and disease self-management was explored in studies conducted by Chenoweth et al. (2008) and Peteet (2002, as cited in Chenoweth et al., 2008). The results from these two studies (Chenoweth et al., 2008; Peteet, 2002, as cited in Chenoweth et al. 2008) suggested that high levels of social support lead to higher levels of self-efficacy, which ultimately predicted increased participation in self-management activities in PD patients. Therefore, it can be concluded that these three variables, social support, self-efficacy, and self-management behaviors, are interrelated and thus should be assessed collectively in chronic disease populations such as PD.

**Summary**

Chapter Two included a detailed literature review of PD, treatments of PD, and the role of the placebo effect in medical interventions. This chapter also discussed the constructs of self-efficacy and social support, the role of these constructs in chronic disease populations such as PD, and how they relate to and influence the placebo effect. The current study was designed to investigate the predictive ability of self-efficacy and social support on physical functioning in PD patients who participated in the parent study and received fetal tissue implantation. The present study explored the influence of baseline levels of self-efficacy and social support on physical improvements at 12- and 24-months post-fetal tissue implantations. This study also examined the influence of baseline levels of self-efficacy and social support on patients’ perceived treatment 12-months after the initial surgery.
Chapter Three: Method

Chapter Three describes the methodology followed in the present study. Information on the participants, procedures, measures, and data analyses is provided.

Participants

**Parent study.** Forty patients with idiopathic Parkinson’s disease (PD) were recruited to participate in a double-blind surgical trial for the parent study conducted by Freed et al. (2001). Twenty patients were randomly assigned to the treatment group to receive fetal tissue implantation and 20 were assigned to the sham surgery group. Those patients in the sham surgery group were given the opportunity to receive the fetal tissue implantation after the blind was lifted 13-months following the initial surgery. The inclusion and exclusion criteria used for the parent study are described in detail below. More complete information describing the parent study can be found in Freed et al. (2001).

**Inclusion criteria.** There were several primary inclusion criteria for participants in the parent study (Freed et al., 2001). First, the patients needed to have been diagnosed with PD for at least seven years, presenting with at least two of the three major signs of PD (bradykinesia, rigidity, and tremor at rest), and demonstrating responsiveness to the L-dopa drug treatment. Specifically, patients needed to demonstrate continued responsiveness to L-dopa, but with reduced benefit. The patients were required to have previously tried other more conservative medical treatments for their PD. Patients were
required to be medically fit to undergo implantation surgery through the certification of their regular physician. Next, the patients needed to demonstrate the presence of an intractable problem that was not controlled by dopamine agonists, such as dyskinesias, “off” periods, or “freezing.” The patients had to be willing to commit and actively participate in all aspects of the ongoing study and have the means to cover any expenses that were not initially covered by the parent study’s NIH grant. Age of the patients was required to be between 20 and 75 years old. As required by NIH, the parent study recruited a participant sample that was racially and ethnically representative of the prevalence rates of PD within each of the racial/ethnic groups. The prevalence rates used were current at the time of participant recruitment. Lastly, imaging results of a magnetic resonance imaging (MRI) scan of the brain in the last 18-months needed to indicate normal function and activity and a flurodopa PET scan needed to be compatible with idiopathic PD.

**Exclusion criteria.** The parent study also included a series of exclusion criteria (Freed et al., 2001). The patients in the parent study could not demonstrate any obvious depression, hallucinations, or cognitive impairments (as assessed by a neuropsychologist). The patients were also excluded if they had a history of previous brain surgery, injury, or exposure to toxins. The presence of any other severe medical diseases, such as diabetes mellitus, cardiopulmonary disease, or cerebrovascular disease, excluded patients from the study. Patients were also excluded from the study if they were taking any neuroleptic medications. Lastly, patients were not accepted into the parent study if they could not receive medical clearance from their regular physician to undergo the surgical procedure (Freed et al., 2001).
Quality of life study. The 40 patients in the parent study were invited to participate in the Quality of Life (QoL) study conducted by McRae et al. (2004); 30 patients agreed to participate. The demographic information for these patients, as calculated by McRae et al. (2004), is presented in Table 1. This information was collected at true baseline and is grouped into the two conditions: treatment and sham surgery group.

Table 1

Demographic Information at True Baseline

<table>
<thead>
<tr>
<th>Demographic Variable</th>
<th>Treatment Group (n = 12)</th>
<th>Sham Surgery Group (n = 18)</th>
<th>Total (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Age (M ± SD)</td>
<td>59.9 ± 7.9</td>
<td>56.3 ± 10.4</td>
<td>57.8 ± 9.5</td>
</tr>
<tr>
<td>Education (M ± SD)</td>
<td>16.6 ± 2.8</td>
<td>16.3 ± 2.2</td>
<td>16.4 ± 2.4</td>
</tr>
<tr>
<td>Duration of disease (M ± SD)</td>
<td>15.5 ± 6.6</td>
<td>16.0 ± 3.6</td>
<td>15.7 ± 5.0</td>
</tr>
<tr>
<td>Married/living with partner</td>
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<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Annual income &gt; $40,000</td>
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<td>10</td>
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<tr>
<td>Currently employed</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Family history of PD</td>
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<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Other chronic health problems</td>
<td>5</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Currently smoke</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ever smoke</td>
<td>2</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Ethnicity</td>
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<td>1</td>
</tr>
<tr>
<td>White</td>
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<td>16</td>
<td>27</td>
</tr>
</tbody>
</table>

Procedures

All data for the present investigation were collected in the original QoL study conducted by McRae et al. (2004) from 1995 to 2000. No new data was collected for the
present study, but rather a secondary data analysis of the data collected by McRae et al. (2004) was conducted. The following is a description of the procedures followed by those researchers.

Data were collected through written questionnaires that were sent to the patients one week after follow-up medical evaluations at the Irving Center for Clinical Research at Columbia-Presbyterian Medical Center (CPMC), now called the New York Presbyterian Hospital. The questionnaires assessed three domains of quality of life: Physical, Emotional, and Social functioning. Patients were provided with envelopes that included pre-paid postage and were asked to return their questionnaires to the researchers. For each completed and returned questionnaire, patients were paid $25. The response rate was 98%. The patients were instructed to respond to the questionnaires and not to have a third party complete the questionnaire on their behalf. The patients’ primary caregivers were also included in the study and were mailed separate questionnaires to complete, which evaluated the patients’ quality of life across the three domains. The data from the caregiver study were not analyzed in the present study.

The patients were medically evaluated two times before the surgery and at 4-, 8-, 12-, and 24-months after surgery. These evaluations lasted between three and four days to allow for an evaluation when the patients were both on and off medications. A neurologist and two research nurses provided medical care to the patients throughout the course of the study; these medical personnel were blind to the treatment group assignments until the blind was lifted approximately 13-months after the initial surgeries.
Measures

Because of the uniqueness of this study and the lack of previous research with persons participating in double-blind clinical trials lasting more than one year, a broad range of measures was administered in order to assess changes over time. These measures were completed by the participants recruited in the original QoL study and were returned to the principal investigator through the mail. As described in the Procedures section, many of these measures were categorized into three main domains of QoL: Physical, Emotional, and Social functioning. The measures can be found in Appendices A through H.

Physical functioning. The patients’ level of Physical functioning was assessed with several measures that are uniformly recognized as assessment tools for patients with PD: the patient version of the Unified Parkinson’s Disease Rating Scale (UPDRS); (Montgomery, Lieberman, Sing, & 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). In addition, a single item called the “Free or Restricted” item was used.

Unified Parkinson’s Disease Rating Scale. Patients’ self-reported level of physical functioning was assessed through the patient version of the Unified Parkinson’s Disease Rating Scale (UPDRS); (Montgomery, Lieberman, Sing, & Fries, 1994). This measure was adapted from the standard neurologist version of this measure (Fahn, Elton, & Members of the UPDRS Development Committee, 1987). The patient version of the UPDRS measures patients’ perception of their physical functioning and overall physical problems related to PD. This measure consists of four primary subscales: Activities of
Daily Living (ADLs) at their “best”, ADLs at their “worst”, Severity of Symptoms at their “best”, and Severity of Symptoms at their “worst.” These qualitative descriptors of “best” and “worst” correspond to the patients’ physical functioning “at their best” and their physical functioning “at their worst.”

The two ADLs subscales include eight items that are scored on a 5-point Likert scale with the following descriptors: 1 (Normal), 2 (Adequate), 3 (Limited), 4 (Need help), and 5 (Unable to do). Each of the scales is scored separately and patients can score a minimum of eight points and maximum of 40 points, with lower scores indicating better physical functioning. The eight activities of daily living that are rated on these subscales are walking, dressing, cutting food, performing personal hygiene tasks, getting up from a chair, turning in bed, writing, and talking.

The two Severity of Symptoms subscales rate five problem areas that are scored on a 5-point Likert scale with the following descriptors: 1 (Normal), 2 (Mild), 3 (Moderate), 4 (Severe), and 5 (Very Severe). Each of these scales is scored separately and the total scores range from five to 25, with lower scores indicating better physical functioning. The five problems rated include tremor, swallowing, salivation, “freezing” when walking, and falling. As discussed in the parent and the QoL study, previous research has demonstrated that the scores “off” medications are a more accurate assessment of the patients’ status, therefore only the “worst” scores were included in the composite variable in the data analysis (Freed et al., 2001; McRae et al., 2004).

The estimate of reliability (Cronbach’s alpha) for the patient version of the UPDRS in this sample ranged from .65 to .90 (McRae et al., 2004). This estimate was re-computed in the preliminary analyses of the present study. The original patient version of.
the UPDRS has demonstrated acceptable construct validity when compared to other widely used measures assessing physical functioning in patients with PD according to Ramaker, Marinus, Stiggelbout, and van Hilten (2002).

*Hoehn and Yahr Stage of Parkinson’s disease scale.* The patients’ stage of disease was assessed with the Hoehn and Yahr Stage of Disease scale (1967), which is a standard rating scale for PD. The patients were asked to rate their stage of disease on a scale ranging from zero to five; 0 (no signs of the disease), 1 (evidence of the disease on one side of the body), 2 (evidence of the disease on both sides of the body; without impairment of balance), 3 (mild to moderate bilateral disease; some postural instability; physically independent), 4 (severe disability; still able to walk or stand unassisted) and 5 (wheelchair bound or bedridden unless aided). The patients provided ratings at a baseline assessment before the surgery and at each of the follow-up assessments (four-, eight-, 12-, 24-, and 36-months). The version of the scale utilized in the QoL study was previously adapted for patient use and was found to correlate with ratings by neurologists (McRae et al., 2002). The estimate of reliability of this measure was assessed within the sample during the preliminary data analyses. Information on the construct validity of this scale was not available. Because this measure was used in the parent study and has been consistently used in previous studies with this data, it was used in the present study.

*Schwab and England Activities of Daily Living scale.* Schwab and England (1967) developed this scale to specifically assess the level of physical functioning of PD patients related to activities of daily living. This scale has been widely used in research studies with this patient population (Goetz, et al., 1989). The scale asks the patients to indicate one response “that best describes your present activity level.” The responses are
graded in 10% increments, from 0% to 100%. Each of these ratings corresponds to a brief qualitative descriptor. For example, 0% corresponds to the following statement, “Vegetative functions such as swallowing, bladder and bowel functions are not functioning. Bed-ridden.” A 50% rating is accompanied with the following description, “More dependent. Help with half of chores, slower, etc. Difficulty with everything.” Lastly, a rating of 100% indicated “Completely independent. Able to do all chores without slowness, difficulty or impairment. Essentially normal. Unaware of any difficulty.” Patients rated themselves on this scale at baseline and each of the follow-up assessments (four-, eight-, 12-, 24-, and 36-months) in the original QoL study. The estimate of reliability of this measure was assessed within the sample during the preliminary data analyses. This measure has demonstrated moderate to substantial validity (Ramaker et al., 2002).

**Free and Restricted Scale.** This scale consists of a single, global item that was used to assess how free or restricted patients feel “in doing what [they] want to do.” The patients in this study rated their functioning using a 7-point rating 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). Lower scores indicated better physical functioning as it relates to quality of life activities. The estimate of reliability of this measure was assessed within the sample during the preliminary data analyses. Information on the construct validity of this single-item scale was not available. Because this measure was used in the parent study and has been consistently used in previous studies with this data, it was used in the present study.

**Emotional functioning.** In the original QoL study, the participants’ level of Emotional functioning was assessed with multiple measures that examined mood, stress,
and the intrusiveness of the patients’ disease. The measures used to assess these aspects of Emotional functioning are not within the scope of the present study and therefore will not be discussed here (please see McRae et al. [2004] for additional information on these scales).

**Self-efficacy.** Self-efficacy is a construct that was assessed in the original QoL study by McRae et al. (2004), but has not been investigated in previous analyses with this data. Therefore, self-efficacy was the primary focus of the present study.

**Self-efficacy Scale.** A measure of self-efficacy was adapted from Lorig et al.’s (1993) previous work with self-efficacy and was used by McRae et al. (2004) for the original QoL study to assess the patients’ level of self-efficacy related to the management of their disease and attending circumstances. Measurement of self-efficacy occurred at baseline and each follow-up assessment. The scope of this assessment was specific to patients’ beliefs about managing various aspects of their chronic disease, PD. This measure was adapted from the work of Lorig et al. (1993) who first investigated self-efficacy among persons with arthritis. Lorig and colleagues have developed several self-management programs for a variety of chronic disease patient populations including those with diabetes, cancer, and chronic obstructive pulmonary disease. The self-efficacy scale used in the QoL study consisted of seven items assessing self-efficacy on a 7-point Likert scale. Each item was prefaced with the phrase, “How certain are you that you can…” Examples of items on the self-efficacy scale include, “do something to help yourself feel better if you are feeling blue?” and “manage your situation so that you can do the things that you enjoy doing?” The scale ranged from 1 (very uncertain) to 7 (very certain) indicating the patients’ level of certainty that they could perform the task
described in the item. Higher scores correspond with higher levels of self-efficacy and lower scores correspond with lower levels of self-efficacy. The estimate of reliability of this measure was assessed within the sample during the preliminary data analyses. Similar measures developed by Lorig et al. (1993) in the chronic disease population have demonstrated acceptable levels of construct validity.

**Social functioning.** The participants’ level of Social functioning was primarily assessed with one measure of perceived social support. The measure used in the original QoL study was the Social Provisions Scale (Cutrona & Russell, 1987).

**Social Provisions Scale.** The Social Provisions Scale was developed by Cutrona and Russell (1987) to measure perceived social support. The scale is 24-items that are measured on a 4-point Likert scale. The scale ranges from 1 (*strongly disagree*) to 4 (*strongly agree*). Total scores on this measure range from 24 to 96, with lower scores corresponding to lower levels of perceived social support. The reliability estimate in the original QoL study at baseline was .91 (Cronbach’s alpha; McRae et al., 2004). This estimate was re-analyzed in the preliminary analyses of the present study. Construct validity for this instrument has been established (Russell et al., 1984).

**Perceived treatment.** 12-months after receiving the initial surgery, those patients who participated in the QoL study were asked to report which treatment, actual neural implantation or sham surgery, they believed they received (McRae et al., 2004). This discrete response of perceived treatment, neural tissue implant or sham surgery, served as a dependent variable in the present study.
Data Analyses

A secondary data analysis was conducted with the data collected from the original QoL study. The analyses had a preliminary analysis stage as well as a primary analysis stage.

Preliminary data analyses were conducted in order to obtain demographic information as well as descriptive statistics. Due to the use of multiple measures of physical functioning, preliminary analyses created a composite variable within the physical functioning domain, which was used in the primary data analyses. The creation of this composite variable served to decrease the number of dependent variables used in the primary analyses and improve the strength of the statistical analyses. Reliability estimates for each of the measures was re-examined prior to the primary analyses. The primary data analyses were conducted in order to answer the following research questions:

1. Are self-efficacy and perceived social support at adjusted baseline correlated with physical functioning at 12- and 24-months post-fetal tissue implantation?

2a. Do self-efficacy and perceived social support at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation? Does the interaction term of social support x self-efficacy at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation?

2b. Do self-efficacy and perceived social support at adjusted baseline predict physical functioning 24-months following fetal tissue implantation? Does the interaction term of social support x self-efficacy at adjusted baseline predict physical functioning of PD patients 24-months following fetal tissue implantation?
3. Do self-efficacy and perceived social support at true baseline predict perceived treatment at 12-months after the initial surgery?

Because patients who originally received the sham surgery were given the opportunity to have the actual fetal tissue implantation once the blind was lifted 13-months after the first surgery, this study examined the patient data at 12- and 24-months after the actual fetal tissue implantation (or 24- and 36-months after the initial surgery for those in the sham surgery group).

The first research question was answered through Pearson’s product moment correlation ($r$). This analysis tested for a linear relationship between self-efficacy and perceived social support at adjusted baseline and physical functioning at 12- and 24-months post-fetal tissue implantation. For the purposes of this analysis, both scales of social support and self-efficacy were considered continuous measures and it was assumed that there was a meaningful difference between each of the values on the rating scales. The following assumptions of Pearson’s product moment correlation were examined: normality and linearity. However, due to the small sample size and unique exploratory nature of the study, violations of these assumptions did not prevent further analyses.

The second set of research questions (2a and 2b) was answered through hierarchical linear regression analyses, as this is the method used to predict the scores on a dependent variable based on values of multiple independent variables. In this case, the analyses tested the ability of two primary independent predictors, self-efficacy and perceived social support at adjusted baseline, to predict the dependent variables, physical functioning at 12- and 24-months post-fetal tissue implantation. For the purposes of these analyses, both scales of social support and self-efficacy were considered continuous.
measures and it was assumed that there is a meaningful difference between each of the values on the rating scales. Additionally, the analyses of physical functioning at 12- and 24-months controlled for patients’ length of PD diagnosis and level of physical functioning at adjusted baseline. In other words, length of PD diagnosis and physical functioning at baseline were considered step one in the regression analyses. The first independent variable of interest, perceived social support at adjusted baseline, was entered independently into the regression analyses and was considered step two. Next, the second independent variable of interest, self-efficacy at adjusted baseline, was added to the regression analyses as step three. It was determined to enter perceived social support into the regression model before self-efficacy based on previous work with this data set, which suggested that social support was a significant predictor of physical functioning in this sample. The present study was principally interested to reveal the unique contribution of self-efficacy to the regression model as well as the interaction between the two constructs, social support and self-efficacy. Finally, a second analysis examined the ability of the interaction between perceived social support and self-efficacy at adjusted baseline to predict physical functioning at 12- and 24-months post-fetal tissue implantation.

Data were screened for outliers on the independent and dependent variables using Mahalanobis distance. The following assumptions of regression were examined: normality of the predictors, homoscedasticity, and linearity. Independence between independent variables was tested. The data were analyzed for multicollinearity and singularity. However, violations of these assumptions did not prevent further analyses, due to the small and unique sample as well as the exploratory nature of the study.

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The third research question was answered using logistic regression. The patients’ perception of treatment at 12-months after the initial surgery was a discrete variable, either neural tissue implant or sham surgery group, and was predicted by two continuous independent variables, self-efficacy and perceived social support at true baseline. This analysis controlled for patients’ length of PD diagnosis and physical functioning at true baseline, which was considered step one. The two variables of interest, self-efficacy and perceived social support at true baseline, were considered step two. Similar to the first set of primary analyses, data were screened for outliers on the independent variables using Mahalanobis distance. The following assumptions of regression were examined: normality of the predictors, and linearity. Independence between independent variables was tested. The data were analyzed for an absence of multicollinearity and singularity. Again, violations of these assumptions did not prevent further analyses, due to the small and unique sample size as well as the exploratory nature of the study.

**Summary**

Chapter Three described the methodology that was used in this study. A description of the participants, procedures, measures, and data analyses was provided. The preliminary and primary data analyses that were used to answer the three main research questions were discussed.
Chapter Four: Results

Overview

Chapter Four presents the results of the statistical analyses directed to the research questions of the present study. A description of the preliminary analyses is provided along with the findings of the primary analyses. All statistical analyses were performed using the Statistical Package for the Social Sciences 21 for Mac (SPSS 21). The statistical analyses used two-tailed tests of significance with the alpha level set at \( p < .1 \) because of the experimental nature of the study and the small sample size.

As previously described, the participants were assigned to one of two treatment groups during the parent study (Freed et al., 2001). Those in the original implant group received fetal tissue implantation during the first surgery (\( n = 20 \)). Of these 20 participants, 12 participated in the QoL study. The second treatment group received a sham surgery initially (\( n = 20 \)) and then had the option of receiving the fetal tissue implantation after the blind was lifted at 13-months. Of these 20 participants, 18 participated in the QoL study.

The first and second research questions posed in the present study required the comparison of QoL variables at baseline, 12-, and 24-months after fetal tissue implantation. Due to the one-year double blind period and the two treatment groups having the implantation at least one year apart, adjustments were made in terms of data entry in order to align the temporal course of the surgeries. Therefore, true baseline
measurements for the sham group collected before the initial sham surgery were substituted with measurements taken 12-months after the initial surgery. These 12-month scores were the most representative of the sham participants immediately before receiving the actual implantation during the second surgery. If the true baseline measurements taken before the initial surgery were used, it would represent the state of participants more than one year prior to receiving the actual tissue implantation. This data shift was performed with all variables for the sham group in order to temporally equate their measurements with the implant group relative to the time the fetal tissue implantation surgery was performed. All of the primary statistical analyses conducted to answer Research Questions 1, 2a, and 2b were performed using this shifted data. It is noted throughout the preliminary analyses and the primary analyses for Research Question 3 when the true baseline measurements (i.e., before the initial surgery) were used; otherwise it should be assumed that all analyses were done with the shifted data.

Preliminary Analyses

Demographic information. As previously discussed in Chapter Three, demographic information had previously been collected on the 30 participants who participated in the QoL study (McRae et al., 2004). Chapter Three presented a summary of the demographic information calculated by McRae et al. (2004). The present study re-calculated these statistics. The re-calculated statistics were identical to those calculated by McRae et al. (2004) and are presented in Table 2. This information was collected before the initial surgery and was grouped into the two conditions: treatment and sham surgery groups.
Table 2

Demographic Information at True Baseline

<table>
<thead>
<tr>
<th>Demographic Variable</th>
<th>Treatment Group (n = 12)</th>
<th>Sham Surgery Group (n = 18)</th>
<th>Total (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: Female</td>
<td>7</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Age (M ± SD)</td>
<td>59.9 ± 7.9</td>
<td>56.3 ± 10.4</td>
<td>57.8 ± 9.5</td>
</tr>
<tr>
<td>Education (M ± SD)</td>
<td>16.6 ± 2.8</td>
<td>16.3 ± 2.2</td>
<td>16.4 ± 2.4</td>
</tr>
<tr>
<td>Duration of disease (M ± SD)</td>
<td>15.5 ± 6.6</td>
<td>16.0 ± 3.6</td>
<td>15.7 ± 5.0</td>
</tr>
<tr>
<td>Married/living with partner</td>
<td>10</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Annual income &gt; $40,000</td>
<td>9</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Currently employed</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Family history of PD</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Other chronic health problems</td>
<td>5</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Currently smoke</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ever smoke</td>
<td>2</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Ethnicity: Asian American</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>African American</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Latino/a</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>White</td>
<td>11</td>
<td>16</td>
<td>27</td>
</tr>
</tbody>
</table>

Descriptive statistics of QoL measures. Descriptive statistics for the QoL measures used in the present study were computed. The means, standard deviations, ranges, sample sizes, skewness values, and kurtosis values for each of the physical functioning measures at adjusted baseline, 12-months post-fetal tissue implantation, and 24-months post-fetal tissue implantation are presented. The descriptive statistics for the physical functioning composite variable are presented at true baseline, adjusted baseline, 12-months post-fetal tissue implantation, and 24-months post fetal tissue implantation, as all four of these time points were used in the primary statistical analyses. Finally, the descriptive statistics for the social support and self-efficacy measures are presented at true baseline and adjusted baseline only, as these are the only time points that were examined in the primary analyses (see Table 3).
Table 3

*Descriptive Statistics of QoL Measures*

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>M</th>
<th>SD</th>
<th>Range</th>
<th>Skewness</th>
<th>Kurtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Functioning</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>(Lower Scores = Better Functioning)</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UPDRS: Activities of Daily Living (at worst)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted Baseline</td>
<td>29</td>
<td>28.69</td>
<td>6.27</td>
<td>13.0 – 40.0</td>
<td>-.32</td>
<td>.22</td>
</tr>
<tr>
<td>12-months post-implantation</td>
<td>23</td>
<td>24.96</td>
<td>6.93</td>
<td>12.0 – 38.0</td>
<td>.07</td>
<td>-.48</td>
</tr>
<tr>
<td>24-months post-implantation</td>
<td>20</td>
<td>21.75</td>
<td>6.03</td>
<td>11.0 – 33.0</td>
<td>.11</td>
<td>-.74</td>
</tr>
<tr>
<td>UPRDRS: Severity of Symptoms (at worst)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted Baseline</td>
<td>30</td>
<td>13.23</td>
<td>2.81</td>
<td>7.0 – 19.0</td>
<td>.08</td>
<td>-.15</td>
</tr>
<tr>
<td>12-months post-implantation</td>
<td>22</td>
<td>12.68</td>
<td>3.59</td>
<td>6.0 – 18.0</td>
<td>-.17</td>
<td>-.93</td>
</tr>
<tr>
<td>24-months post-implantation</td>
<td>20</td>
<td>11.80</td>
<td>4.16</td>
<td>6.0 – 22.0</td>
<td>.72</td>
<td>.30</td>
</tr>
<tr>
<td>Free or Restricted Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted Baseline</td>
<td>30</td>
<td>4.73</td>
<td>1.48</td>
<td>2.0 – 7.0</td>
<td>-.66</td>
<td>-.50</td>
</tr>
<tr>
<td>12-months post-implantation</td>
<td>22</td>
<td>4.09</td>
<td>1.69</td>
<td>2.0 – 7.0</td>
<td>.17</td>
<td>-1.49</td>
</tr>
<tr>
<td>24-months post-implantation</td>
<td>20</td>
<td>3.45</td>
<td>1.57</td>
<td>1.0 – 6.0</td>
<td>.33</td>
<td>-.82</td>
</tr>
<tr>
<td><strong>Physical Functioning</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite Score (z-scores)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>True Baseline</td>
<td>29</td>
<td>.00</td>
<td>2.40</td>
<td>-6.56 – 4.21</td>
<td>-.42</td>
<td>.54</td>
</tr>
<tr>
<td>Adjusted Baseline</td>
<td>29</td>
<td>.19</td>
<td>2.30</td>
<td>-5.35 – 4.95</td>
<td>-.16</td>
<td>.03</td>
</tr>
<tr>
<td>12-months post-implantation</td>
<td>28</td>
<td>.09</td>
<td>2.51</td>
<td>-4.86 – 4.95</td>
<td>.001</td>
<td>-.65</td>
</tr>
<tr>
<td>24-months post-implantation</td>
<td>20</td>
<td>.17</td>
<td>2.53</td>
<td>-5.41 – 5.48</td>
<td>-.15</td>
<td>.57</td>
</tr>
<tr>
<td><strong>Social Functioning</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>(Higher Scores = Better Functioning)</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Provisions Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>True Baseline</td>
<td>27</td>
<td>80.41</td>
<td>9.17</td>
<td>58.0 – 96.0</td>
<td>-.16</td>
<td>-.04</td>
</tr>
<tr>
<td>Adjusted Baseline</td>
<td>29</td>
<td>79.72</td>
<td>9.98</td>
<td>67.0 – 96.0</td>
<td>.17</td>
<td>-1.65</td>
</tr>
<tr>
<td><strong>Self-Efficacy</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>(Higher Scores = Better Functioning)</em></td>
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<td></td>
</tr>
<tr>
<td>Self-Efficacy Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>True Baseline</td>
<td>29</td>
<td>37.86</td>
<td>7.74</td>
<td>19.0 – 49.0</td>
<td>-.53</td>
<td>-.007</td>
</tr>
<tr>
<td>Adjusted Baseline</td>
<td>29</td>
<td>37.21</td>
<td>7.61</td>
<td>19.0 – 49.0</td>
<td>-.33</td>
<td>-.12</td>
</tr>
</tbody>
</table>
Reliability of variables used to answer primary research questions. The reliability estimates, specifically Cronbach’s $\alpha$, were calculated for each of the scales used to answer the research questions in this study. These estimates were calculated as part of the preliminary analyses in order to examine the internal consistency of the measures. The reliability estimates at true baseline for these scales are presented in Table 4. The Free and Restricted variable was a single-item scale and therefore a reliability estimate was not calculated. Although the UPDRS Severity of Symptoms at Worst scale was not in the acceptable range, it was used in the primary analyses because it has been consistently used in previous work with these data. Item analysis revealed that Item 1 of this scale, “Tremor,” was negatively related to the other items in the scale. The item analyses suggested that if Item 1 “Tremor” and Item 3 “Salivation” were removed from the scale, the reliability estimate would be in the acceptable range at true baseline. Further analyses of this scale demonstrated that the reliability estimate increased at 12- and 24-month follow-up (12-month: Cronbach’s $\alpha = .64$, 24-month: Cronbach’s $\alpha = .88$). Furthermore, tremor and salivation are cardinal symptoms of PD and therefore it was important that these symptoms were accounted for in the measurement of physical functioning. Therefore, it was decided to include all five items of the UPDRS Severity of Symptoms at Worst Scale in the primary analyses. All other scales had reliability estimates in the acceptable range of .7 (Nunnally, 1978).

Correlations of QoL variables. Pearson’s (r) correlations were calculated in order to examine the linear relationships between the QoL variables. The relationships
between the physical functioning variables at true baseline were examined as well as the
to baseline were investigated using Pearson’s product moment correlation. As displayed in
Table 5, strong, positive linear relationships existed between the Free and Restricted
Scale and the Activities of Daily Living at Worst Scale \((r = .50, p < .01)\) as well as the
Severity of Symptoms at Worst Scale and the Activities of Daily Living at Worst Scale \((r
= .59, p < .01)\). A moderate, positive linear relationship existed between the Free and
Restricted Scale and the Severity of Symptoms at Worst Scale \((r = .296, p = .12)\). The
strength and direction of these relationships provided justification to combine them and
create a composite variable for the physical functioning domain.
The administration of the Schwab and England Activities of Daily Living Scale (Schwab & England, 1967) changed during the course of the QoL study and therefore a consistent score for this measure was not available at each data collection period. For this reason, the Schwab and England scale was not included in the physical functioning composite variable despite the strong correlations with other measures of physical functioning (see Table 5). This was consistent with previous work done with this data set.

Table 5

*Pearson Correlation Coefficients for Physical Functioning QoL Variables at True Baseline*

<table>
<thead>
<tr>
<th></th>
<th>Free or Restricted</th>
<th>Activities of Daily Living at Worst</th>
<th>Severity of Symptoms at Worst</th>
<th>Schwab and England</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free or Restricted</td>
<td>Pearson Correlation</td>
<td>.50</td>
<td>.296</td>
<td>-.56</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td>.006***</td>
<td>.12</td>
<td>.002***</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>Activities of Daily Living at Worst</td>
<td>Pearson Correlation</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>Severity of Symptoms at Worst</td>
<td>Pearson Correlation</td>
<td>.59</td>
<td>.991***</td>
<td>.991***</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td>.001***</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>Schwab and England</td>
<td>Pearson Correlation</td>
<td>-.42</td>
<td>-.32</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td>.025**</td>
<td>.090*</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>

Note. *p < .1  **p < .05  ***p < .01.
Data for the Hoehn and Yahr Stage of Parkinson’s Disease scale (Hoehn & Yahr, 1967) were not available at true baseline and therefore were not examined in the correlation analyses and were not included in the physical functioning composite variable.

Pearson’s (r) correlation analyses were conducted in order to examine the linear relationships between the measures of social support and self-efficacy at true baseline. Assumptions of Pearson’s product moment correlation were met. Specifically, no univariate outliers were identified and the variables of interest, social support and self-efficacy, were considered to be continuous variables. As displayed in Table 6, a strong, positive linear relationship existed between perceived social support and self-efficacy (r = .42, p < .05).

Table 6

*Pearson Correlation Coefficients for Self-efficacy and Social Support at True Baseline*

<table>
<thead>
<tr>
<th></th>
<th>Social Provisions Scale</th>
<th>Self-efficacy Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Provisions Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Self-efficacy Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>.42</td>
<td>1</td>
</tr>
<tr>
<td>Significance</td>
<td>.030**</td>
<td>N/A</td>
</tr>
<tr>
<td>N</td>
<td>27</td>
<td>29</td>
</tr>
</tbody>
</table>

Note. *p < .1 ** p < .05.

**Creation of the composite variable.** As presented in Table 5, there were strong correlations between the following measures of physical functioning: Free and Restricted Scale, Activities of Daily Living at Worst Scale, and Severity of Symptoms at Worst
Scale. Therefore these measures were combined to create one composite variable to represent the physical functioning domain. This was done for each of the following time points: true baseline, adjusted baseline, 12-months post-fetal implantation, and 24-months post-fetal implantation. Please see the section entitled “Overview” in this chapter for a description of how and why the data were shifted to adjust for the different surgery dates within the treatment groups. Scores for each of the measures were standardized at each period based on the mean and standard deviation of that measure at that time period. The standard scores for each measure were then combined to create a total z-score that comprised the composite variable. A reliability estimate, specifically Cronbach’s α, was then calculated for the physical functioning composite variable at the adjusted baseline (Cronbach’s α = .65). While this reliability estimate is not above the acceptable range of .7 (Nunnally, 1978), it was decided to use the composite variable in the primary analyses because it approached the acceptable range and has been used in previous work with these data.

**Primary Analyses**

The previous section presented demographic information, descriptive statistics of the QoL variables, reliability estimates, correlations of the QoL variables, and a description of how the composite physical functioning variable was created. This section presents the results of the primary analyses that were conducted in order to answer the research questions of the study. All statistical analyses used two-tailed tests of significance and the alpha level was set at $p < .1$ because of the experimental nature of the study and the small sample size.
**Research question 1.** Are self-efficacy and perceived social support at adjusted baseline correlated with physical functioning at 12- and 24-months post-fetal tissue implantation?

As previously discussed, all data were adjusted to account for the two treatment groups and the fetal tissue implantation surgeries that occurred one year apart. Therefore, “adjusted baseline” measures of self-efficacy and social support represented measurements 12-months before participants received the actual implantation. Likewise, the physical functioning scores at 12- and 24-months represented measurements recorded 12- and 24-months after the real implantation occurred, not from the date of the initial surgery, as the sham group did not receive the actual fetal tissue implantation until the second surgery.

Assumptions of Pearson’s product moment correlation were met. Specifically, no univariate outliers were identified and the variables of interest, self-efficacy at adjusted baseline, social support at adjusted baseline, and physical functioning at 12- and 24-month follow-up, were considered to be continuous variables.

The linear relationships between self-efficacy and perceived social support at adjusted baseline and the physical functioning composite variable at 12- and 24-months post-fetal tissue implantation were investigated using Pearson’s product moment correlation. As displayed in Table 7, a strong, positive linear relationship existed between self-efficacy and perceived social support at adjusted baseline ($r = .43, p < .05$). A strong, negative linear relationship was observed between self-efficacy at adjusted baseline and physical functioning at 12-months post-fetal tissue implantation ($r = -.43, p < .05$). A strong, positive linear relationship existed between physical functioning at 12- and 24-
months post-fetal tissue implantation ($r = .54, p < .05$). Social support did not demonstrate strong, linear relationships with the physical functioning composites at 12- or 24-months post-fetal tissue implantation (see Table 7).

Table 7

*Pearson Correlation Coefficients for Self-efficacy and Social Support at Adjusted Baseline and Physical Functioning Composite at 12- and 24-months Post-fetal Tissue Implantation*

<table>
<thead>
<tr>
<th></th>
<th>z-score: Self-efficacy at Adjusted Baseline</th>
<th>z-score: Social Support at Adjusted Baseline</th>
<th>z-score: Physical Functioning Composite at 12-months</th>
<th>z-score: Physical Functioning Composite at 24-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td>.43</td>
<td>-.43</td>
<td>-.23</td>
</tr>
<tr>
<td>Significance</td>
<td>N/A</td>
<td>.02**</td>
<td>.02**</td>
<td>.34</td>
</tr>
<tr>
<td>N</td>
<td>29</td>
<td>29</td>
<td>28</td>
<td>20</td>
</tr>
</tbody>
</table>

Note. * $p < .1$  ** $p < .05$. 

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Research question 2a. Do self-efficacy and perceived social support at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation?

A hierarchical multiple regression analysis was conducted in order to answer Research Question 2a. This analysis controlled for the patients’ length of PD diagnosis and level of physical functioning at adjusted baseline. In other words, these control variables comprised step one of the regression analysis. Perceived social support at adjusted baseline was entered into the analysis as step two. Self-efficacy at adjusted baseline was entered into the model as step three. It was determined to enter perceived social support into the regression model before self-efficacy based on previous work with this data set, which suggested that social support was a significant predictor of physical functioning in this sample. The present study was principally interested to examine the unique contribution of self-efficacy to the regression model as well as the interaction between the two constructs, social support and self-efficacy.

All assumptions of multiple regression were tested and met. Specifically, a review of the histograms and skewness and kurtosis values determined that the independent and dependent variables were normally distributed. The control variable, patients’ length of PD diagnosis, was slightly positively skewed, but was still included in the analyses as multiple regression is robust to assumption violations such as this. The assumption of homoscedasticity was met, as the distribution of the standardized residuals along the fit line appeared to be constant. Scatterplots examining the relationship between the independent and the dependent variables appeared linear, and therefore this assumption of multiple regression was met. The data were screened and no multivariate outliers were
identified. Finally, the variance inflation factor demonstrated that the independent variables were not multicollinear.

The regression model, with adjusted baseline levels of self-efficacy and social support as predictors, was found to be statistically significant, $R^2(4,23) = .63, \ p < .001$. Therefore, 63.0% of the variance in the physical functioning composite scores 12-months post-fetal tissue implantation was explained by self-efficacy and social support levels at adjusted baseline when the patients’ length of PD diagnosis and physical functioning scores at adjusted baseline were controlled. The regression model was not significantly improved with the addition of step two, or social support at adjusted baseline. It was not until step three was added, or self-efficacy at adjusted baseline, that the regression model was significantly improved. See Table 8 below for details. Of the two predictors, self-efficacy was significant and contributed more to the prediction of physical functioning at 12-months ($\beta = -.30, \ p < .1$) than social support ($\beta = .14, \ p = .35$). Specifically, the model and the slopes of the predictors suggested that as self-efficacy scores at baseline increased, physical functioning scores 12-months post-fetal tissue implantation decreased, or in other words, improved. As total scores on the social support scale at baseline increased, the physical functioning composite scores at 12-month follow-up also increased, or in other words, worsened (lower scores on the physical functioning composite suggested better functioning).

The control variables, patients’ length of PD diagnosis ($\beta = .24, \ p < .1$) and physical functioning at adjusted baseline ($\beta = .64, \ p < .001$), were also found to be statistically significant predictors of physical functioning 12-months post-fetal tissue implantation.
A second hierarchical multiple regression analysis was conducted in order to further explore Research Question 2a: Does the interaction term of self-efficacy x perceived social support at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation? This analysis controlled for the patients’ length of PD diagnosis and level of physical functioning at adjusted baseline. In other words, these control variables comprised step one of the regression analysis. An interaction term was calculated for perceived social support and self-efficacy at adjusted baseline. The interaction term was calculated by multiplying the centered values (score – mean) of the social support and self-efficacy variables at adjusted baseline. The interaction term and the centered social support and self-efficacy variables were entered into the analysis as step two.

Table 8

*Hierarchical Multiple Regression Analyses Predicting Physical Functioning 12-months Post-Fetal Tissue Implantation From Social Support and Self-efficacy*

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Physical Functioning 12-months Post-Fetal Tissue Implantation</th>
<th>( R^2 )</th>
<th>( \Delta R^2 )</th>
<th>Adjusted ( R^2 )</th>
<th>( \beta )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1: Control Variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td>.56***</td>
<td>.56***</td>
<td>.53***</td>
<td>.22</td>
<td></td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
<td></td>
<td></td>
<td>.71***</td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td>.56***</td>
<td>.001</td>
<td>.51***</td>
<td>.22</td>
<td></td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
<td></td>
<td></td>
<td>.71***</td>
<td></td>
</tr>
<tr>
<td>Social Support</td>
<td></td>
<td></td>
<td></td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td>.63***</td>
<td>.065*</td>
<td>.56***</td>
<td>.24*</td>
<td></td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
<td></td>
<td></td>
<td>.64****</td>
<td></td>
</tr>
<tr>
<td>Social Support</td>
<td></td>
<td></td>
<td></td>
<td>.14</td>
<td></td>
</tr>
<tr>
<td>Self-efficacy</td>
<td></td>
<td></td>
<td></td>
<td>-.30*</td>
<td></td>
</tr>
</tbody>
</table>

Note. * \( p < .1 \)  ** \( p < .05 \)  *** \( p < .01 \)  **** \( p < .001 \).
The regression model, with centered social support, centered self-efficacy, and the centered interaction term as predictors, was statistically significant, $R^2(5,22) = .63$, $p < .001$. However, this model was not a significant improvement from the regression model comprised of only the control variables. See Table 9 below for details. The interaction term was not found to be a statistically significant predictor of physical functioning 12-months post-fetal tissue implantation ($\beta = -.07$, $p = .63$).

As previously described, the control variable physical functioning at adjusted baseline ($\beta = .66$, $p < .001$) was a statistically significant predictor of physical functioning 12-months post-fetal tissue implantation. The control variable, patients’ length of PD diagnosis ($\beta = .23$, $p = .10$), was not statistically significant (see Table 9).

Table 9

*Hierarchical Multiple Regression Analyses Predicting Physical Functioning 12-months Post-Fetal Tissue Implantation From Interaction Term Social Support x Self-efficacy*

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Physical Functioning 12-months Post-Fetal Tissue Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$R^2$</td>
</tr>
<tr>
<td>Step 1: Control Variables</td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td>.56****</td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td>.63****</td>
</tr>
<tr>
<td>PD Duration</td>
<td></td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
</tr>
<tr>
<td>Centered Social Support</td>
<td></td>
</tr>
<tr>
<td>Centered Self-efficacy</td>
<td></td>
</tr>
<tr>
<td>Centered Interaction Term</td>
<td></td>
</tr>
<tr>
<td>Social Support x Self-efficacy</td>
<td></td>
</tr>
</tbody>
</table>

Note. * $p < .1$  ** $p < .05$  *** $p < .01$  **** $p < .001$.

**Research question 2b.** Do self-efficacy and perceived social support at adjusted baseline predict physical functioning 24-months following fetal tissue implantation?
A hierarchical multiple regression analysis was run in order to answer Research Question 2b. This analysis controlled for the patients’ length of PD diagnosis and level of physical functioning at adjusted baseline; these control variables comprised step one of the regression analysis. Similar to Research Question 2a, perceived social support at adjusted baseline was entered into the analysis as step two. Self-efficacy at adjusted baseline was entered into the model as step three. Again, it was determined to enter perceived social support into the regression model before self-efficacy based on previous work with this data set, which suggested that social support was a significant predictor of physical functioning in this sample. The present study was principally interested to examine the unique contribution of self-efficacy to the regression model as well as the interaction between the two constructs, social support and self-efficacy.

All assumptions of multiple regression were tested and met. Specifically, a review of the histograms and skewness and kurtosis values determined that the independent and dependent variables were normally distributed. The control variable, patients’ length of PD diagnosis, was slightly positively skewed, but was still included in the analyses as multiple regression is robust to assumption violations such as this. The assumption of homoscedasticity was met, as the distribution of the standardized residuals along the fit line appeared to be constant. Scatterplots examining the relationship between the independent and the dependent variables appeared linear, and therefore this assumption of multiple regression was met. The data were screened and no multivariate outliers were identified. Finally, the variance inflation factor demonstrated that the independent variables were not multicollinear.
The regression model, with baseline levels of self-efficacy and social support as predictors, was not statistically significant, $R^2(4,15) = .36$, $p = .13$, although the model comprised of the control variables, length of PD diagnosis and physical functioning at adjusted baseline, was significant (see Table 10). The control variable, physical functioning at adjusted baseline ($\beta = .57$, $p < .05$) was found to be a statistically significant predictor of physical functioning 24-months post-fetal tissue implantation; length of PD diagnosis ($\beta = -.15$, $p = .48$) was not statistically significant. See Table 10 for details.

Table 10

*Hierarchical Multiple Regression Analyses Predicting Physical Functioning 24-months Post-Fetal Tissue Implantation From Social Support and Self-efficacy*

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Physical Functioning 24-months Post-Fetal Tissue Implantation</th>
<th>$R^2$</th>
<th>$\Delta R^2$</th>
<th>Adjusted $R^2$</th>
<th>$\beta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1: Control Variables</td>
<td></td>
<td>.28*</td>
<td>.28*</td>
<td>.19*</td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-.11</td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.51**</td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td>.34*</td>
<td>.07</td>
<td>.22*</td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td></td>
<td></td>
<td></td>
<td>-.16</td>
<td></td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
<td></td>
<td></td>
<td>.60**</td>
<td></td>
</tr>
<tr>
<td>Social Support</td>
<td></td>
<td></td>
<td></td>
<td>.28</td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td></td>
<td>.36</td>
<td>.01</td>
<td>.19</td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td></td>
<td></td>
<td></td>
<td>-.15</td>
<td></td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
<td></td>
<td></td>
<td>.57**</td>
<td></td>
</tr>
<tr>
<td>Social Support</td>
<td></td>
<td></td>
<td></td>
<td>.33</td>
<td></td>
</tr>
<tr>
<td>Self-efficacy</td>
<td></td>
<td></td>
<td></td>
<td>-.13</td>
<td></td>
</tr>
</tbody>
</table>

Note. * $p < .1$ ** $p < .05$.

A second hierarchical multiple regression analysis was conducted in order to further explore Research Question 2b: Does the interaction term self-efficacy x perceived social support at adjusted baseline predict physical functioning 24-months following fetal...
tissue implantation? This analysis controlled for patients’ length of PD diagnosis and level of physical functioning at adjusted baseline. In other words, these control variables comprised step one of the regression analysis. As previously described, an interaction term was calculated for perceived social support and self-efficacy at adjusted baseline. The interaction term was calculated by multiplying the centered values (score – mean) of the social support and self-efficacy variables at baseline. The interaction term and the centered social support and self-efficacy variables were entered into the analysis as step two.

The regression model, with centered social support, centered self-efficacy, and the centered interaction term as predictors, was not statistically significant, $R^2(5,14) = .44$, $p = .11$, although the model comprised of the control variables, length of PD diagnosis and physical functioning at adjusted baseline, was significant (see Table 11). The interaction term was not found to be a statistically significant predictor of physical functioning 24-months post-fetal tissue implantation ($\beta = .32$, $p = .18$). As previously described, the control variable, physical functioning at adjusted baseline ($\beta = .43$, $p < .1$) was found to be a statistically significant predictor of physical functioning 24-months post-fetal tissue implantation; length of PD diagnosis ($\beta = -.07$, $p = .76$) was not statistically significant. See Table 11.

**Research question 3.** Do self-efficacy and perceived social support at true baseline predict perceived treatment at 12-months after the initial surgery?

A binary logistic regression was conducted in order to answer Research Question 3. Because the blind was lifted 13-months after the initial surgery, this analyses used true baseline values for one of the control variables, physical functioning, as well as for the
two predictors of interest, social support and self-efficacy. This analysis controlled for patients’ length of PD diagnosis and level of physical functioning at true baseline.

Table 11

**Hierarchical Multiple Regression Analyses Predicting Physical Functioning 24-months Post-Fetal Tissue Implantation From Interaction Term Social Support x Self-efficacy**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Physical Functioning 24-months Post-Fetal Tissue Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$R^2$</td>
</tr>
<tr>
<td>Step 1: Control Variables</td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td>.28*</td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
</tr>
<tr>
<td>PD Duration</td>
<td>.44</td>
</tr>
<tr>
<td>Baseline Physical Functioning</td>
<td></td>
</tr>
<tr>
<td>Centered Social Support</td>
<td></td>
</tr>
<tr>
<td>Centered Self-efficacy</td>
<td></td>
</tr>
<tr>
<td>Centered Interaction Term</td>
<td></td>
</tr>
<tr>
<td>Social Support x Self-efficacy</td>
<td></td>
</tr>
</tbody>
</table>

Note. * $p < .1$  ** $p < .05$.

The predictors of interest at true baseline, self-efficacy and social support, were not found to be significant predictors of perceived treatment group 12-months after the initial surgery. Likewise, the control variables, patients’ length of PD diagnosis and level of physical functioning at true baseline, were not found to be significant predictors of perceived treatment group at 12-months. See Table 12. While it was not statistically significant, social support at true baseline was the strongest predictor of perceived treatment of those variables included in the model (Wald = .98, $p = .33$). The addition of self-efficacy and social support to the regression model comprised of control variables did not significantly improve prediction of perceived treatment group at 12-month follow-up ($\chi^2 = 2.55, p = .64$). The prediction model, including social support and self-
efficacy, accounted for 13.5% of variance in perceived treatment (Nagelkerke $R^2 = .135$) and the model was found to provide good fit ($\chi^2 = 10.49, p = .23$).

Table 12

*Logistic Regression Analyses Predicting Perceived Treatment 12-months After Initial Surgery From Social Support and Self-efficacy at True Baseline*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Perceived Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Constant</td>
<td>.74</td>
</tr>
<tr>
<td>Length of PD Diagnosis</td>
<td>-.04</td>
</tr>
<tr>
<td>Physical Functioning at True Baseline</td>
<td>.19</td>
</tr>
<tr>
<td>Self-efficacy at True Baseline</td>
<td>-.06</td>
</tr>
<tr>
<td>Social support at True Baseline</td>
<td>-.49</td>
</tr>
<tr>
<td>$\chi^2$</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td></td>
</tr>
</tbody>
</table>


**Summary**

Chapter Four presented the results of the statistical analyses conducted to examine the research questions of the present study. A description of the preliminary analyses was provided and followed by the findings of the primary analyses. Chapter Four included each of the following subsections: a) demographic information; b) descriptive statistics of QoL measures; c) reliability of variables used to answer research questions; d) correlations of QoL variables; e) creation of the composite variable; f) primary results for Research Question 1; g) primary results for Research Question 2a; h) primary results for Research Question 2b; and i) primary results for Research Question 3.

Results of the analyses for Research Question 1 revealed strong, linear relationships between self-efficacy at adjusted baseline with the physical functioning composite at 12-months post-fetal tissue implantation. The analyses did not reveal strong,
linear relationships between perceived social support at adjusted baseline with the physical functioning composites at 12- or 24-months post-fetal tissue implantation.

Results of Research Question 2a revealed that self-efficacy at adjusted baseline was a significant predictor of physical functioning 12-months post-fetal tissue implantation. Specifically, as self-efficacy scores increased, physical functioning scores decreased or, in other words, improved. Social support was not found to be a significant predictor of physical functioning 12-months post-fetal tissue implantation. Moreover, it was observed that as total scores on the social support scale increased, the physical functioning composite score also increased or, in other words, worsened (lower scores on the physical functioning composite suggested better functioning). The interaction term, social support x self-efficacy, was not a significant predictor of physical functioning at 12-months post-fetal tissue implantation.

Results of the analyses for Research Question 2b suggested that adjusted baseline levels of social support and self-efficacy were not significant predictors of physical functioning 24-months post-fetal tissue implantation. Likewise, the interaction term, social support x self-efficacy, was not a significant predictor of physical functioning 24-months post-fetal tissue implantation.

Finally, results for Research Question 3 revealed that social support and self-efficacy scores at true baseline were not significant predictors of patients’ perceived treatment group 12-months after the initial surgery, or before the blind was lifted at the 13-month follow-up.
Chapter Five will discuss the conclusions and clinical implications of the statistical results presented in Chapter Four. Chapter Five will also present the limitations of the present study and recommendations for future research.
Chapter Five: Discussion

Overview

Chapter Five presents a summary of the present study, a discussion of the study results, clinical implications of the study findings, limitations of the study, and recommendations for future research.

Summary of the Present Study

Few studies have comprehensively explored the benefit of fetal tissue implantation in PD patients (Lindvall et al., 2004). In particular, researchers have not identified the factors that make patients good candidates for this surgical intervention with the exception of age, as discussed in Freed et al.’s investigation (2001). Variables that likely contribute to positive outcomes following the surgical procedure have not been explored. Similarly, few studies have investigated the mechanisms through which potential benefits of fetal tissue implantation likely operate (Lindvall et al., 2004; McRae et al., 2004). This type of investigation is necessary in order to better understand how and why some participants in a double-blind investigation of fetal tissue implantation for PD improved following the surgical procedure while others did not (Freed et al., 2001). This sort of study informs future surgical interventions with PD patients and assists in selecting candidates who might benefit more than others. Furthermore, this information assists in determining domains of patient life that may require preliminary intervention or
improvement prior to undergoing an invasive surgical procedure such as fetal tissue
implantation.

The present study attempted to address this gap in the literature by exploring the
relationship of self-efficacy and social support with physical functioning in PD patients
following fetal tissue implantation. In particular, this study examined the relationships
between self-efficacy, social support, physical functioning, and perceived treatment in a
sample of PD patients who either received fetal tissue implantation at the start of the
parent study or a sham surgery followed by actual fetal tissue implantation (Freed et al.,
2001). The goal of the present investigation was to contribute to the literature by
examining the role of self-efficacy and social support in regard to physical functioning
and perceived treatment observed in PD patients following fetal tissue implantation.

Data for the present study were collected during a QoL life study conducted by
McRae et al. (2004) that sampled PD patients who participated in a double-blind
investigation of fetal tissue implantation (Freed et al., 2001). Thirty of the 40 patients
who participated in Freed et al.’s (2001) parent study agreed to participate in the QoL
study. Data related to a variety of QoL variables were collected at baseline, four-, eight-,12-, 24-, and 36-month follow-up assessments. The present study examined the predictive
ability of self-efficacy and perceived social support at adjusted baseline on patients’
physical functioning at 12- and 24-month assessments following fetal tissue implantation.
Because patients who originally received the sham surgery were given the opportunity to
have the actual fetal tissue implantation once the blind was lifted 13-months after their
initial surgery, the present study examined patient data at 12- and 24-months after the
actual fetal tissue implantation (or at 24- and 36-months after the initial surgery for those in the sham group). The following research questions were investigated:

1. Are self-efficacy and perceived social support at adjusted baseline correlated with physical functioning 12- and 24-months post-fetal tissue implantation?

2a. Do self-efficacy and perceived social support at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation? Does the interaction term of social support x self-efficacy at adjusted baseline predict physical functioning of PD patients 12-months following fetal tissue implantation?

2b. Do self-efficacy and perceived social support at adjusted baseline predict physical functioning 24-months following fetal tissue implantation? Does the interaction term of social support x self-efficacy at adjusted baseline predict physical functioning of PD patients 24-months following fetal tissue implantation?

3. Do self-efficacy and perceived social support at true baseline predict perceived treatment 12-months after the initial surgery?

**Overall Findings**

The first research question was exploratory in nature and designed to describe the relationships between the two variables of interest, perceived social support and self-efficacy, and physical functioning in the study sample. A composite variable was created for physical functioning to account for the various measures used in the QoL study to assess participants’ overall level of physical functioning (McRae et al., 2004). As anticipated, the results revealed strong, linear relationships between self-efficacy at adjusted baseline with the physical functioning composite variable at 12-months post-fetal tissue implantation. While there were some variable relationships that did not
demonstrate strong correlations, such as social support with physical functioning at 12- or 24-months post-fetal tissue implantation, the theoretical and empirical literature indicates that the variables of interest, social support and self-efficacy, do in fact influence physical functioning (Backer, 2000; Brod et al., 1998; Chenoweth et al., 2008; Taylor, 2003). For this reason, along with the experimental nature of the study, the decision was made to proceed with the regression analyses proposed in research questions two and three.

The second set of research questions were designed to examine the predictive ability of social support and self-efficacy in regard to physical functioning of study participants at 12- and 24-months after receiving fetal tissue implantation. As has been discussed, the analyses examined physical functioning 12- and 24-months after the actual fetal tissue implantation, not from the time of the initial surgery. Therefore, data for the participants who initially received the sham surgery were obtained from follow-up assessments at 12- and 24-months after they received the actual fetal tissue implantation, or at 24- and 36-months following the initial surgery. Likewise, for those who first received the sham surgery, scores of social support and self-efficacy at 12-months from the initial surgery were used as the “adjusted baseline” scores, rather than the true baseline measured at participants’ entry into the study. The reason for this was to investigate relationships over the period from pre-implantation to 12- and 24-months post-fetal tissue implantation.

The results for Research Question 2a revealed that self-efficacy at adjusted baseline was a significant predictor of physical functioning at 12-months post-fetal tissue implantation. As anticipated, when self-efficacy scores increased, physical functioning scores at 12-month follow-up decreased or improved. Social support was not found to be
a significant predictor of physical functioning 12-months following fetal tissue implantation. Moreover, the direction of the relationship observed in this study between social support and physical functioning was not anticipated based on the literature. Specifically, as total scores on the perceived social support scale increased, the physical functioning composite score at 12-month follow-up also increased or, in other words, worsened since lower scores on the physical functioning composite suggested better functioning. This result was not expected based on the literature, rather it was anticipated that as baseline levels of perceived social support increased, physical functioning at 12-month follow-up would decrease or improve. This unexpected finding is likely explained by the small sample size used in the present study. A larger participant sample may demonstrate the pattern of variable relationships anticipated from the literature and reveal that higher levels of perceived social support predict better physical functioning in patients following a surgical intervention such as fetal tissue implantation (Backer, 2000; Taylor, 2003). An interaction term was created to examine the collective ability of social support and self-efficacy to predict physical functioning 12-months post-fetal tissue implantation. The interaction term, social support by self-efficacy, was not found to be a significant predictor of physical functioning at 12-months post-fetal tissue implantation. Based on a review of the theoretical literature describing the interrelationship between these two constructs, this result was not expected (Chenoweth et al., 2008; Kaşikçi & Alberto, 2007).

Results of the analyses for research question 2b indicated that adjusted baseline levels of social support and self-efficacy were not significant predictors of physical functioning at 24-months post-fetal tissue implantation. Likewise, the interaction term,
social support by self-efficacy, was not found to be a significant predictor of physical functioning at 24-months post-fetal tissue implantation. Therefore, it seems that within this PD sample, the ability of self-efficacy to predict physical functioning following fetal tissue implantation was observed at the 12-month follow-up but was not maintained by the 24-month follow-up.

Finally, the third research question was designed to determine if true baseline scores of social support and self-efficacy were predictive of patients’ perceived treatment before the blind was lifted 13-months after the initial surgery. The results revealed that social support and self-efficacy scores were not significant predictors of perceived treatment group at 12-months, an unanticipated result based on the literature (Crow et al., 1999; Howard, 2008; Kaptchuk et al., 2008; Miller et al., 2009).

**Clinical Implications**

The present study demonstrated the important role of self-efficacy as a predictor of physical functioning 12-months after fetal tissue implantation. Specifically, higher levels of self-efficacy were predictive of better physical functioning. Surprisingly, the relationship observed between social support and physical functioning was not in the anticipated direction. Theoretical literature suggested that higher levels of perceived social support would be predictive of better physical functioning, not worse physical functioning which was observed in the present study (Backer, 2000; Taylor, 2003). Other studies examining QoL variables in this participant sample have suggested that social support continues to be an important predictor of physical functioning more than 10 years after fetal tissue implantation (Fazio, 2008).
One possible explanation for this finding may be that a third variable not included in the analyses, specifically negative affectivity, mediated the relationship between perceived social support and physical functioning. The prevalence of depression in the PD population has been estimated between 40-50% and is associated with many poor outcome variables, such as quality of life, progression of physical symptoms, and ability to care for oneself (Ravina et al., 2007; Schrag, 2006). In fact, depression is considered to be the most common neuropsychiatric problem in patients with PD (Papapetropoulos, Ellul, Argyrio, Chroni, & Lekka, 2006). Some literature argues for a more organic cause, citing examples of depression that occurred before the onset of motor symptoms (Papapetropoulos et al., 2006). While other literature contends that the psychosocial and environmental stressors that are associated with a chronic disease, such as PD, influence its development (Papapetropoulos et al., 2006). Regardless of its etiology, depression has adverse effects on quality of life. The negative or maladaptive cognitive styles associated with depression may influence how PD patients perceive their social support and subsequently influence their physical functioning.

Therefore, despite the direction of the relationship observed in the present study between social support and physical functioning, the significant findings of the present study, in conjunction with other follow-up studies with this participant sample, argue that medical research should examine social support and self-efficacy as predictors of physical functioning following surgical interventions such as fetal tissue implantation. Benefits of social support and self-efficacy are extensively recognized and studied in psychological research, but these variables are not examined as consistently in medical research. If variables such as perceived social support and self-efficacy are maximized,
patients may demonstrate a greater responsiveness to these types of medical interventions.

As previously discussed, psychological interventions have been developed to increase levels of self-efficacy in the chronic disease population (Ritter, Lee, & Lorig, 2011; Lorig et al., 2001). Results from these studies demonstrate multiple beneficial health outcomes due to increased self-management self-efficacy, such as decreased disability, fewer medical visits, and less fatigue, and they appear to be maintained over time (Ritter, Lee, & Lorig, 2011; Lorig et al., 2001). Few studies have examined the role of self-efficacy in the management of PD; however, there is some evidence that suggests that there are beneficial effects of high levels of self-efficacy on the management of PD (Chenoweth et al., 2008; Peteet, 2002, as cited in Chenoweth, et al., 2008; Montgomery et al., 1994). Results from the present study are consistent with the findings of the few studies that have examined the role of self-efficacy in management of PD. Although self-efficacy was found to predict physical functioning only at 12-months after fetal tissue implantation, these findings have clinical implications. The results suggest that psychological interventions intended to increase PD patients’ self-efficacy, such as those developed by Lorig et al. (2001), may enhance patient responsiveness to surgery and other medical interventions and may improve their overall disease management.

**Limitations of the Present Study**

The present study includes several limitations. The sample size of the present study (N= 30) was small, as it was identical to the original sample used in the QoL study (McRae et al., 2004). The participant sample for the QoL study was drawn from the parent study. Because of the unique nature of the surgical procedures used in the study
design, the parent study only recruited 40 participants (Freed et al., 2001). This small sample size limits the generalizability of the study’s findings and clinical implications. Particularly, findings from the present study cannot be generalized to the PD population at large due to the unique design of this study and the unusual participant sample who agreed to receive experimental brain surgery for the treatment of their disease. The individuals who volunteered to participate in the parent study, which included the use of a sham surgical procedure, are not likely representative of the PD population at large. Therefore, conclusions from the present study cannot be generalized outside of the individuals who participated in the study. Furthermore, due to the small sample size the decision was made to set the alpha level at .10 for all statistical analyses. This alpha level increases the chance of Type I error, or incorrectly rejecting the null hypothesis, and is another limitation of the present study. Furthermore, the small sample size of this study decreased the overall power of the statistical analyses and thus increased the chance of Type II error, or failing to reject the null hypothesis.

Research questions for the present study were assembled in consideration of new developments in surgical procedures for PD, such as deep brain stimulation (DBS). However, conclusions from the present study are limited due to the unique study design and cannot be generalized to PD patients who are treated with other surgical procedures, such as DBS. Nevertheless, examining baseline levels of social support and self-efficacy as a routine part of pre-surgical evaluations for PD patients may be an important area of future research. A discussion of topics for future research will be provided in the following section.
**Recommendations for Future Research**

In consideration of the study’s findings and clinical implications, several areas for future research have been identified. First, it is recommended that future studies use larger sample sizes in order to expand the external validity or generalizability of their conclusions. However, it is unlikely that the unique nature and conditions of the present study would be replicated in future studies.

Second, it is recommended that future studies examining the effects of surgical procedures for PD patients continue to investigate the QoL variables that were examined in the present study. Specifically, the present study has indicated that baseline levels of self-efficacy have an impact on physical functioning 12-months after surgery; therefore, future studies might consider examining the influence of these QoL variables on physical functioning in patients who are treated with new surgical interventions for PD. For example, a European research consortium named TRANSEURO (2013) is currently conducting a study examining the efficacy of fetal cell-based treatments in PD patients. The results of the present study argue that the researchers with TRANSEURO (2013) examine the role of QoL variables, such as social support and self-efficacy, in their study in order to maximize patient responsiveness to the fetal tissue implantation. The unexpected results of the perceived social support predictor in the present study appear to indicate the need for a more thorough investigation of the domain of emotional functioning and its relationship to social functioning in the prediction of physical functioning in the PD population.

Finally, future research studies might also consider developing and examining the effectiveness of interventions that improve patients’ perceived social support and self-
efficacy before undergoing invasive surgical procedures. These interventions have the potential to increase patients’ responsiveness to surgery and therefore improve their overall physical functioning and quality of life. While the findings of the present study did not suggest that the interaction between social support and self-efficacy was a significant predictor of physical functioning, the literature on these two constructs contend that they may be interrelated (Chenoweth et al., 2008; Cutrona & Russell, 1987; Kaşikçi & Alberto, 2007). This interrelationship suggests that the two constructs should be examined collaboratively, especially among chronic disease populations like PD. Therefore it is recommended that future research continue to collectively examine social support and self-efficacy as potential predictors of physical functioning and overall disease management.

Conclusions

The present study examined the predictive ability of baseline levels of perceived social support and self-efficacy on physical functioning and perceived treatment in a sample of PD patients who received fetal tissue implantation. The study uniquely contributed to the literature, as it was the first to examine the role of self-efficacy and social support within the participant sample as well as the interaction between self-efficacy and social support on physical functioning and perceived treatment.

The study concluded that self-efficacy was a significant predictor of physical functioning at 12-months post-fetal tissue implantation. Social support was not found to be a significant predictor of physical functioning. These QoL variables were not found to be significant predictors of physical functioning at 24-months post-fetal tissue implantation or of perceived treatment group 12-months after the initial surgery. Future
research studies might consider examining the longitudinal role of social support and self-efficacy on patient responsiveness to and benefit from surgical interventions as well as the efficacy of clinical interventions designed to enhance these QoL variables in PD patients prior to surgical interventions.
References


Cersosimo & Benarroch, (2012). Autonomic involvement in Parkinson's disease:

Pathology, pathophysioloogy, clinical features and possible peripheral biomarkers.

*Journal of Neurological Sciences, 313*, 57-63.

Clarkson, E. D. (2001). Fetal tissue transplanation for patients with Parkinson’s disease:

A database of published clinical results. *Drugs and Aging, 18*(10), 773-785.


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)

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

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

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

Severity of Symptoms

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

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

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

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

Hoehn and Yahr Stage of Parkinson’s disease Scale

Using the scale below, please indicated the number that best describes the present stage of your Parkinson’s disease: ____________

0 = No signs of disease.

1 = Evidence of disease on one side of the body (unilateral disease).

2 = Evidence of disease on both sides of the body (bilateral disease), without impairment of balance.

3 = Mild to moderate bilateral disease; some postural instability; physically independent.

4 = Severe disability; still able to walk or stand unassisted.

5 = Wheelchair bound or bedridden unless aided.
## Appendix D

### Free or Restricted Scale

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

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

120
Appendix E

Schwab and England Activities of Daily Living Scale

On the scale below, check the one response that best describes your present activity level.

______ 100% I feel completely independent. I am able to do all chores without slowness, difficulty or impairment. I feel essentially normal. I am unaware of any difficulty.

______ 90% I feel completely independent. I am able to do all chores, but I have some degree of slowness, difficulty or impairment. It might take twice as long. I am beginning to be aware of my difficulty.

______ 80% I feel completely independent in most tasks. However, it takes me twice as long. I am conscious of difficulty and slowness.

______ 70% I do not feel that I am completely independent. I have difficulty with some chores. It takes me three to four times as long to complete some tasks. I must spend a large portion of the day performing tasks.

______ 60% I feel as though I am somewhat dependent. I can do most chores, but I do them exceedingly slowly and with much effort. I sometimes make errors and some tasks are impossible.

______ 50% I feel pretty dependent. I help with about half of my daily tasks and I complete these tasks at a very slow pace. I have difficulty with everything.

______ 40% I feel very dependent. I am able to assist with all tasks, but can do few things alone.

______ 30% Now and then, with a great deal of effort I can begin or complete a few chores alone; however, I need a lot of help.

______ 20% I can do nothing alone. I can be a slight help with some tasks. I am a severe invalid.

______ 10% I am totally dependent and helpless. I am a complete invalid.
Appendix F

Self-Efficacy Scale

How certain are you that you can:

1. Do something to help yourself feel better if you are feeling blue?
   1  2  3  4  5  6  7
   Very uncertain       Very certain

2. Deal with frustration that is often part of having Parkinson’s disease?
   1  2  3  4  5  6  7
   Very uncertain       Very certain

3. Manage your situation so that you can continue to do the things you enjoy doing?
   1  2  3  4  5  6  7
   Very uncertain       Very certain

4. Make some positive changes in your life?
   1  2  3  4  5  6  7
   Very uncertain       Very certain

5. Handle the emotional ups and downs of having Parkinson’s?
   1  2  3  4  5  6  7
   Very uncertain       Very certain

6. Give support to others?
   1  2  3  4  5  6  7
   Very uncertain       Very certain

7. Receive support from others?
   1  2  3  4  5  6  7
   Very uncertain       Very certain
Appendix G

Social Provisions Scale (SPS)

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

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. There are people I can depend on to help me if I really need it.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>2. I feel that I do not have close personal relationships with other people.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>3. There is no one I can turn to for guidance in times of stress.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
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</tr>
<tr>
<td>4. There are people who depend on me for help.</td>
<td>_____</td>
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</tr>
<tr>
<td>5. There are people who enjoy the same social activities I do.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>6. Other people do not view me as competent.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
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</tr>
<tr>
<td>7. I feel personally responsible for the well-being of another person.</td>
<td>_____</td>
<td>_____</td>
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</tr>
<tr>
<td>8. I feel part of a group who share my attitudes and beliefs.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>9. I do not think other people respect my skills and abilities.</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>10. If something went wrong, no one would come to my rescue.</td>
<td>_____</td>
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<td>_____</td>
<td>_____</td>
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<td></td>
</tr>
<tr>
<td>11. I have close relationships that provide me with a sense of emotional security and well-being.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. There is someone I could talk to about important decisions in my life.</td>
<td></td>
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</tr>
<tr>
<td>13. I have relationships where my competence and skill are recognized.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. There is no one who shares my interests and concerns.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. There is no one who really relies on me for their well-being.</td>
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<tr>
<td>16. There is a trustworthy person I could turn to for advice if I were having problems.</td>
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<td>17. I feel a strong emotional bond with at least one other person.</td>
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<tr>
<td>18. There is no one I can depend on for aid if I really need it.</td>
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<tr>
<td>19. There is no one I feel comfortable talking about problems with.</td>
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<tr>
<td>20. There are people who admire my talents and abilities.</td>
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<tr>
<td>21. I lack a feeling of intimacy with another person.</td>
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</tbody>
</table>

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Appendix G, continued

Social Provisions Scale (SPS)

<table>
<thead>
<tr>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>22. There is no one who likes to do the things I do.</td>
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<tr>
<td>23. There are people I can count on in an emergency.</td>
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<tr>
<td>24. No one needs me to care for them.</td>
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</tbody>
</table>
Appendix H

Participant Demographics

INFORMATION ABOUT YOU

1. Gender: (check one)   _____Male   _____Female

2. Age: ________

3. What is your racial/ethnic background? (check one)
   _____ Native American   _____ Black   _____ White
   _____ Hispanic   _____ Asian   _____ Other

4. How many years of school have you completed? (circle last year completed)

   HIGH SCHOOL   YEARS OF COLLEGE/VOCATIONAL SCHOOL
   9 10 11 12  1 2 3 4 5 6 more than 6

5. 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

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

7. If you are married to your partner, how long have you been married? ______

8. If you are married, is this your: (check one)
   _____ first marriage
   _____ second marriage
   _____ third marriage
9. Do you have paid employment right now? (check one)

_____No
_____Yes, part-time
_____Yes, full-time

10. Do you currently do any volunteer work?

_____Yes
_____No
_____I used to, but no longer do

11. 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): ________________________________________

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

_____Yes If yes, please describe: _______________________________________ 
_____No