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Illness Impact and Adjustment to Parkinson's Disease: Before and After Treatment with Tolcapone

Mickie D. Welsh DNSc, RN
University of San Diego

ILLNESS IMPACT AND ADJUSTMENT TO PARKINSON'S DISEASE: BEFORE AND AFTER TREATMENT WITH TOLCAPONE

by

Mickie D. Welsh RN

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ILLNESS IMPACT AND ADJUSTMENT TO PARKINSON'S DISEASE:

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There is evidence that adjustment to chronic illnesses such as Parkinson's disease (PD) may be affected by psychological factors especially how patients appraise and cope with the stress of their illness. There has been limited research available examining the role of illness impact or appraisal in adjustment to chronic illness. No studies were found dealing with the inter-relationship of illness impact, adjustment and pharmacological treatment.

The purpose of this study was to determine whether the quality of life (as conceptualized by impact of illness and adjustment) was improved by treatment with tolcapone in persons with Parkinson's disease. This study was done in parallel with a double-blind placebo controlled study of the efficacy and safety of tolcapone.

Quality of life was measured by the Sickness Impact Profile (SIP) and adjustment to Parkinson's disease by the Psychosocial Adjustment to Illness Scale (PAIS-SR).

Illness impact and adjustment to Parkinson's disease were improved across all treatment groups when compared to

patients who received placebo. Total illness impact was significantly improved ($p = .003$), physical illness impact was significantly improved ($p = .05$) and psychosocial illness impact was significantly improved ($p = .007$) in patients who received tolcapone when compared to placebo.

Adjustment to illness was not significantly different in the tolcapone group when compared to patients receiving placebo. however a dose related improvement response was found.

DEDICATION

This dissertation is dedicated to Cheryl H. Waters M.D. and "our" patients with Parkinson's Disease. Without Cheryl's professional and personal support this study would not have been possible. Her steadfast support and encouragement have helped me through the highs and lows of this study. Cheryl's professionalism, dedication and caring,and her clinical expertise serve as a continual model of excellence in professional practice. To "our" patients with Parkinson's disease whose tenacity and spirit never fail to touch me and whose everyday experience with this illness have taught me the importance of quality of life.

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CHAPTER I

INTRODUCTION

Parkinson's Disease (PD), a chronic, degenerative, neurologic condition affects approximately 1% of the aged population. Parkinson's Disease is characterized by loss of neurons in the substantia nigra and other pigmented nuclei (Langston, Koller and Giron, 1992). Death of these specialized cells results in striatal dopamine deficiency, the primary neurochemical lesion of PD. Symptoms of idiopathic PD, the most common of the akinetic-rigid syndromes, include tremor, poverty of movement (akinesia), slowness and fatiguing (bradykinesia), postural instability and rigidity (Weiner and Lang, 1989).

The complexity of motor dysfunction characteristic of Parkinson's Disease results in diminution of many aspects of movement. These impairments have far reaching consequences which affect independent activities of daily living, employment, role fulfillment, self concept and a myriad of interpersonal interactions. The decline in functional

ability in PD can change robust and strong individuals into stooped and frail ones. PD can change confident and independent persons into depressed and dependent ones, or persons who were bright and alert can become apathetic and listless. The social burden of Parkinson's Disease symptoms is a heavy one. For the individual with this diagnosis, life is fraught with frustration, embarrassment and loneliness (Koller, 1987). Because of its progressive nature, PD eventually results in varying degrees of loss of an individual's independent functional ability. Adjustment to such changes presents the patient and family with enormous challenges.

The unique manner in which individuals and families deal with the demands of this progressive illness influences the degree and nature of lifelong adjustment and well-being. Though it is not possible to reverse the physical changes resulting from Parkinson's Disease, cognitive appraisal of the threat and personal resources may help to moderate the impact of the illness (Miller, 1992). Coping with the everyday problems that face individuals with Parkinson's Disease may be the greatest challenge (Hutton & Dipel, 1989).

Effective coping strategies utilized by individuals with Parkinson's Disease are critical to successful adjustment to this disabling disease. Learning to cope with an illness such as Parkinson's Disease requires great determination and a positive attitude (Crary & Waters, 1989). Coping however may be linked to the individuals cognitive appraisal of the illness as a threat. Little is known about Parkinson patients' appraisal of this diagnosis as a threat or the impact this diagnosis and its'symptoms have on the individual or their families' functioning.

We are largely ignorant of how patients see themselves as having changed for better or for worse by their illness or its' treatment methods. The mediating factors that act as buffers against psychological distress and how the patient's social environment affects and is affected by illness needs further study (Dakof & Mendelsohn, 1984).

In order for nurses to assist patients and family members to successfully optimize the quality of their life experiences, it is critical to understand the impact of this illness. Despite the multiple medical problems associated with PD, the basic human needs of the patient must be met effectively if a successful process of adjustment and

rehabilitation is to be achieved. The challenge to nursing, medicine and pharmacological therapy is to sustain a quality of life through moderation of physical symptoms, while maintaining and sustaining personal and family function and relationships which provide support and nurture effective adaptive processes.

The mainstay pharmacological treatment for Parkinson's Disease is a form of replacement therapy, a levodopa/ carbidopa (L-dopa) combination which reduces disease symptoms by chemically replacing the neurotransmitter dopamine. However, despite pharmacological treatment, a steady decline in motor function inevitably ensues. Long term therapy with levodopa eventually results in diminished efficacy, dose-related motor fluctuations and the development of side effects. Though treatment with L-dopa decreases mortality and subdues motor symptoms, it does not reverse the decline in social functioning (Koller, 1987).

Recent interaction studies of levodopa in healthy volunteers have suggested that a new medication, tolcapone, when given together with levodopa, may result in the need for lower doses of levodopa, and provide prolonged efficacy

of levodopa and potentially fewer side effects. Although there exists partially effective drug therapy for the symptoms of PD, the length and quality of the PD patient's life also depends on the maintenance of social and role fulfillment. Patients' quality of life and adaptation are clearly affected by both the disease and its treatment (Fitzsimmons and Bunting, 1993).

There currently exists an abundance of literature describing the effect of pharmacological and surgical interventions on motor and depressive symptoms in patients with Parkinson's Disease. There is also a large body of conceptual nursing knowledge concerning the impact of chronic illnesses. However, relatively few investigators have dealt with the psychosocial aspects of living with PD. Even less attention has been paid to the interaction of pharmacological treatment, functional ability, illness impact and adjustment (Levin & Weiner, 1987).

For a comprehensive understanding of Parkinson's Disease, we need to broaden our perspective on this illness to "include the psychosocial aspects which may provide buffers against both the physical and psychological stressors imposed by chronic illness" (Dakof & Mendelsohn,

1986, p. 385). To determine such a perspective includes understanding how an individual patient and their family experiences and adjusts to their illness. Such a comprehensive approach would broaden the perspective on this disabling disease to include the critical psychosocial component without sacrificing the enormous advantages of the biomedical approach (Dakof & Mendelsohn, 1986).

The primary purpose of this study was to determine if patients with PD would experience decreased impact of illness and improved psychosocial adjustment to their illness after treatment with tolcapone. The secondary purpose of this study was to reveal the clinical significance of subjective non-disease specific indicators, quality of life, as critical outcome variables for clinical practice and research.

This study was done in parallel with a primary double-blind placebo-controlled clinical trial which was conducted to determine the safety and efficacy of three doses of tolcapone when compared to patients receiving a placebo (inactive substance).

Theoretical Framework

The theoretical framework supporting this study is the cognitive theory of psychological stress and coping of Lazarus and Folkman (1984). Coping has long been recognized as playing a central role in human adaptation. From this theoretical perspective, coping is the process of managing demands (external or internal) that are appraised as taxing or exceeding the resources of a person. An important component of this theory is its focus on process and management rather than mastery of demands facing an individual. This component is critically important when studying chronic illnesses such as Parkinsons's disease which present patients with lifelong problems that can't be mastered but can be managed, redefined or tolerated for optimal adaptation (Folkman & Lazarus, 1984). This perspective is a necessary one for advanced practice nurses working in clinical and research practice settings with chronic illness populations such as Parkinson's Disease.

From this transactional theoretical view, individuals are in dynamic, mutually reciprocal relationships with their environment. Such relationships include interactions between the individual and other individuals and the institutions

representing his or her sociocultural environment. Such interactions are usually achieved through loosely prescribed behavioral patterns termed roles. The functional efficiencies of an individual's role behaviors (e.g., spouse, parent, professional) tend to be highly correlated with judgments concerning his or her levels of psychosocial adjustment (Derogatis & Derogatis, 1990).

Stressful situations which the individual faces, such as chronic illness, are appraised as either taxing or exceeding one's resources and therefore posing a threat or danger to well being. Long term outcomes are moderated by two processes: cognitive appraisal and coping.

Cognitive appraisal represents an evaluative process of sources of stress as either harm, threat or challenge. The appraisal of stressors assists an individual's ability to produce a positive outcome or, in the case of Parkinson's Disease, to promote optimal adaptation. Lazarus and Launier (1978) maintain that the determining feature of response to a stressor is the individual's appraisal of the situation.

If individuals are able to cope effectively with the problems they face, they may be able to reduce the harmful consequences of the stressors (McCrae, 1986). Coping is

required to overcome damage or loss, to prevent things from getting worse, to come to terms with the situation as it is, or to reinterpret the meaning of the stressor.

In this study, the theory of coping and adaptation of Lazarus and Folkman was utilized to frame the context of the role of the impact of Parkinson's Disease, as a harmful stressor, and psychosocial adjustment before and after a pharmacological intervention. This theoretical framework provides the foundation for examining unique outcome measures, illness impact and psychosocial adjustment, in a study of a pharmacological intervention. Lazarus and Launier's perspective of cognitive appraisal of a stressor (such as Parkinson's Disease) as either harm, threat or challenge provides support for introduction of the subjective patient perspective into a traditionally disease oriented approach. Such a theoretical view brings together the nursing (person oriented) and medical (disease oriented) and research perspectives to develop empirical knowledge necessary to aid patients struggling to manage the stresses of disabling disease (Lazarus, et al, 1984).

Research Hypotheses

The following hypotheses were tested to determine whether the impact of and adaptation to Parkinson's Disease is improved after treatment with tolcapone:

1. Total illness impact will be significantly lower in individuals with Parkinson's Disease who receive tolcapone as compared to patients receiving a placebo (inactive substance).
2. Physical illness impact will be significantly lower in individuals with Parkinson's Disease who receive tolcapone as compared to patients receiving a placebo (inactive substance).
3. Psychosocial illness impact will be significantly lower in individuals with Parkinson's Disease who receive tolcapone as compared to those receiving a placebo (inactive substance).
4. Psychosocial adjustment to illness will be significantly improved in Parkinson's patients receiving tolcapone as compared to those receiving a placebo (inactive substance).

Definition of Terms

Two major concepts were the focus of this study: impact of illness, and psychosocial adjustment to illness. The theoretical definitions of these variables were as follows.

Impact of Illness

The impact of illness is the unique blend of psychological and somatic sensations imposed by a chronic illness which upsets or stresses people (Haan, 1982). Impact of illness was operationalized in this study subjectively by the Sickness Impact Profile (SIP) (Bergner 1977) and objectively by the Unified Parkinson's Disease Rating Scale (Fahn et Elton, 1987).

Psychosocial Adjustment to Illness

Psychosocial adjustment to illness is the quality of a patient's psychosocial adjustment to a current medical illness or its residual effects. Psychosocial adjustment to illness was operationalized by the Psychosocial Adjustment to Illness Scale (PAIS-SR) (Derogatis & Derogatis, 1983).

Summary

Chapter I focused on the concepts of impact of illness and psychosocial adjustment to illness as critical components in the assessment and treatment of individuals

with Parkinson's Disease. Traditionally, emphasis has been placed on an objective disease specific focus. The role and importance of psychosocial status in overall well being and quality of life as a critically important variable for measuring outcome in clinical studies and for determining clinical improvement has been suggested. The need and importance of subjective (patient) measurement of improvement in addition to objective determination of disease specific measurement has been stressed.

CHAPTER II

Review Of The Literature

Theoretical discourse on the stress-coping-adjustment paradigm has been prolific. The existence of the relationships between the impact of illness (stress), appraisal of illness and coping has been acknowledged in an extensive body of literature (Lazarus & Folkman, 1984, Folkman, Lazarus, Gruen and De Longis, 1986). However, since the generalizability of the entire paradigm to the patient with Parkinson's Disease has yet to be confirmed, this study focused primarily on the illness impact, cognitive appraisal-adjustment relationship. The impact of a chronic illness may be even more exaggerated in illnesses which result in limitations in movement. Limitations in movement have far reaching consequences which considerably effect issues of personal independence, role fulfillment, self esteem and ultimately psychosocial adjustment. Because the symptoms are very obvious in illnesses effecting movement, patients often feel stigmatized by their symptoms. Therefore

comparisons with hypertension or heart disease populations for example do not provide equal comparison groups. The effect of chronic illness and adjustment in diseases with limitations in movement, and in Parkinson's Disease in specific will be addressed.

The Impact of Illness in Diseases Affecting Movement

Illness imposes severe, acute, chronic or recurrent conditions of psychological stress (Lazarus, 1978). Current theory and research on the relationship between stressful events and indicators of adaptational status such as somatic health and psychological symptoms reflect the belief that this relationship is mediated by coping processes (Folkman, Lazarus, Gruen and De Longis, 1986).

Several approaches have been used to attempt to identify the mechanisms by which the stress-adaptational process is mediated. Theoretical approaches have considered personality characteristics, the characteristics of the stressful situation itself and generalized coping strategies applied to all stressful situations.

Though age at diagnosis and disease course varies, Rheumatoid Arthritis (RA) and Multiple Sclerosis (MS) samples are often compared to patients with Parkinson's

Disease because of the similar changes in motoric function, and the degenerative course of the illness.

Physical health status, personality and interpersonal functioning of patients with Multiple Sclerosis were studied by Zeldou and Pavlou (1988). Illness impact measured by the Sickness Impact Profile (SIP) was greatest in the physical domain (m = 24.6) followed by total impact (m = 21.1) and psychosocial impact (m = 17.41). In this study, significant differences were found between men and women. Thirteen of 18 correlations between physical impact scales and interpersonal functioning scales were significantly different for women compared to 0 of 18 correlations in men. However male subjects reported much greater illness impact on social interaction (m = 23.20) than females (m = 14.54, t = 2.26, p = <.03). A significant correlation between age and physical illness impact was also found (r = .35, p = <.01) and total illness impact (r = .30, p = <.01). Differences by sex in this study suggested further opportunity for inquiry. The disproportionate sample size of women to men may have accounted for these findings, however actual differences in illness impact may exist by gender.

The role of illness impact, coping responses, and degree of disability of 20 Multiple Sclerosis (MS) patients was studied by Buelow (1991). Patients rated fatigue and uncertainty about the future as most stressful, while needing help eating or dressing and visual changes were the least stressful. Degree of disability did not appear to correlate with stressors (r = .149). However, a positive correlation was found between uncertainty about the future and fatalistic coping style (r = .52, p = <.01) and a negative correlation between depression and optimistic coping (r= -.155, p = <.01). Cautious interpretation of these findings must be used however as patients were hospitalized and possibly felt more secure and less stressed. In addition, participants were treated with steroids, often associated with feelings of euphoria which might have confounded the results.

The possible relationship of two types of stressors, life events and illness experience, to three sets of attitudes, life satisfaction, self assessed coping and satisfaction with treatment was examined in 97 randomly selected outpatients with multiple sclerosis (Counte, Bielauskas, and Pavlou, 1983). Personal life satisfaction

was measured using the Life Satisfaction Index, and coping was measured by the MS Adjustment Scales. Life satisfaction was related to hospitalization, (f = 11.7, p = <.001), to anxiety (f = 22.6, p = <.001), to age (f = 3.8, p = <.001), and to life stress (f = 5.9, p = <.001). Negative associations of these variables and personal life satisfaction accounted for 45% of the explained variance. Higher personal life satisfaction scores were thus found among patients who were less anxious, younger, those experiencing fewer stressors and had fewer hospitalizations. These findings reflected a sample of MS patients with less disease severity and disease duration which might account for these findings.

To characterize the impact of rheumatoid arthritis (RA) in terms of physical and psychosocial changes, Deyo, Inui, Leininger and Overman (1982) studied seventy-nine patients in four functional categories of RA. Participants completed the Sickness Impact Profile (SIP) to determine the impact of their disease on physical and psychosocial functioning. When compared with 624 individuals from a large pre-paid health plan, RA patients had greater mean illness impact (Total SIP scores) 15.6 when compared to health plan member controls

3.6. The SIP physical and psychosocial dimension scores were reported to be positively correlated (r = .478, p = <.001) in this study. The authors interpreted these correlations to mean that at a given point in time, a decrease in physical function is accompanied by altered psychosocial status. However, since these are subscales of the same instrument, and are calculated together to determine overall illness impact, correlations would be expected and may not necessarily be interpreted as concomitant indicators of physical and psychosocial change indicative of illness at a given point in time. This criticism would seem to be appropriate when authors report of the relationship of SIP scores to functional categories of American Rheumatism Association (disease severity) was examined. Overall SIP and Physical Dimension subscale scores increased with increased disease severity, however, psychosocial dimension scores increased mildly from class 1 to 2 (less disease severity), but decreased in class 3 (mild disease severity), while in class 4 scores (moderate disease severity) psychosocial function remained the same as it had in class 2 disease severity. These findings suggested that a linear

relationship may not have existed between psychosocial function and increasing disease severity in this sample.

The Impact of Parkinson's Disease

A phenomenologic study of six patients with PD by Marr (1991) revealed 4 major themes of the illness: a) impact of disease (also described as loss), b) dealing with the disease (social interaction losses), c) maintaining independence, and d) effort. Though the study sample is small, it provided qualitative support for the concept of disease impact in the lives of individuals with PD.

A study to examine the effects of levodopa on activity, social participation, depression and enjoyment of life was performed by Singer (1976) soon after the discovery of levodopa therapy. Singer studied 169 patients, 149 before 9 months treatment with levodopa and 20 who served as controls. Singer concluded that levodopa therapy did not reverse but rather conserved the decline in social functioning, considered a corollary of PD. After treatment with levodopa, symptom improvement and others expectations, (r = .246, p = <.05), (r = .217, p = <.05) were significantly related to enjoyment of life respectfully. Social participation was related to symptom improvement, (r = .224,

p = <.05), disease severity, (r = -.308, p = <.01), disease duration (r = .25, p = <.01) and sick role attitudes, (r = .30, p = <.01). Overall, only 2 of 15 variables significantly contributed to post-treatment effect. The author suggested symptom improvement resulting from treatment with levodopa appeared to be independent of patients' initial level of social and psychological functioning. Unfortunately this study does not clarify the specific operationalization of the sociopsychological variables in terms of measurement, validity, reliability or evaluative properties. Findings therefore, may not have met measurement standards for evaluative properties.

Starkstein, Mayberg, Preziosi and Robinson (1992) studied the relationship of depression, cognitive decline and impairment in functional ADL in a sample of 105 individuals with PD. Patients were grouped on the basis of psychiatric evaluation into major, minor or no depression categories. The patients with major depression showed a significantly greater cognitive decline (f = 4.36, p = <.05) and deterioration in functional ADL (f = 3.26, p = <.05) than either the minor or non-depressed group.

The impact of chronic illness was studied in 145 PD patients, 735 ET (Essential Tremor) patients and 87 age matched community controls by Busenbark, Nash, Hubble and Koller (1991). The SIP was used to compare the impact of illness related dysfunction in these samples. Patients with Parkinson's Disease had much higher illness impact scores (total SIP 19.0) when compared to patients with Essential Tremor (9.2) and controls (3.4). Similar findings were reported in both the physical and psychosocial dimension scores. Psychosocial scores were higher in PD patients (20.2), when compared to controls (3.6), and in essential tremor patients (11.7). Physical dimension scores were similarly highest in PD (17.7), control (2.3), and essential tremor (9.2). When Parkinson's Disease patients were compared with essential tremor and controls, total score, dimension scores and subscale scores were all significantly different ranging from $p = <.0001$ to $<.05$.

In a preliminary study of 12 PD patients and their spouses, PD patients' impact of illness correlated significantly ($r = .41$ $p <.01$) with duration of illness and disease stage ($r = 0.42$, $p = <.02$) when compared with

controls who had no significant correlations (Kurlan, Barold, Page, Como & Shoulson 1989).

Longstreth, Nelson, Linde and Munoz (1992), studied 44 patients with PD and 44 age and sex-matched controls to determine the utility of the SIP in PD. The SIP (total score) correlated with the Hoehn and Yahr (r = .59, p = <.001) and the Columbia Scale (r = .54, p =.001). Significant differences were found between the PD and control groups on the SIP (16.8, p = <.001), physical dimension (r = 12.9, p <.005) and psychosocial dimension (r = 19.4, p = <.001). The authors concluded that the SIP could be used to supplement PD-specific disability scales to provide a broad measure of functional status in PD as well as a promise of documentation of functional changes that occur with treatment.

In exploring the relationships between aspects of physical illness (clinical severity, Hoehn and Yahr and functional disability) 136 Parkinsons patients were studied by MacCarthy and Brown (1989). Self-esteem, coping style and practical support contributed significantly to the variance in psychological adjustment. The authors concluded that well-being in patients with Parkinson's is not exclusively

dependent on a simple relationship between disability and depression and that other factors should be taken into account in the clinical management of the illness.

A controlled trial of piracetam in the treatment of intellectually impaired patients with Parkinson's Disease was conducted by Sano, Stern, Marder and Mayeux, (1990). The SIP was used to assess functional status in these patients and was completed by a family member living with the study patient. The authors reported a significant improvement in the SIP (total) score in the piracetam group compared with the placebo group ($p < .05$).

The stress of chronic illness in conditions affecting movement and PD in particular was illustrated by the studies presented. Patients with PD consistently reported both physical and psychosocial stress from their illness. Only the studies of Sano et al.(1990) and Singer (1976) were evaluative, all other studies were discriminative in nature.

Psychosocial Adjustment to Chronic Illness

Increasing numbers of individuals surviving longer with chronic illnesses have shifted the focus of interest from mortality to long term morbidity. The demands made by such illnesses on the coping skills, psychological integrity, and

social supports of these patients has brought the significance of psychosocial adjustment into bold relief (Derogatis & Derogatis, 1990).

A general model of appraisal, coping and adjustment in patients with rheumatoid arthritis (RA) was developed by Smith and Wallston (1992). Based on the theory of Lazarus and Folkman, a causal model was used to test the short and long term adaptation consequences of coping as well as the antecedent variables (appraisals, beliefs, social support, and disease activity) that promote particular coping styles. They concluded that interventions designed to bolster a generalized sense of competence and to discourage helplessness appraisals and passive coping strategies in response to pain, have the potential to improve the psychological adjustment and functional well being of individuals facing chronic illness.

Cassileth, Lusk, Strouse, Miller, Brown, Cross and Tenaglia (1984) studied 758 chronically ill individuals and concluded that adaptation to chronic illness was independent of a particular diagnosis. In the six diagnostically different groups studied no statistically significant differences in psychological status emerged. However

patients whose ambulation was affected had lower scores on the dependent variable Mental Health Index (MHI scores). Although this study seemed to suggest that diagnostic category and severity of disease are independent of adaptation, the populations studied may not have been comparable when impairment of motor function is more carefully considered.

Felton, Revenson and Hinricksen (1984) studied 170 patients with diabetes, rheumatoid arthritis, arthritis, cancer and hypertension. Using a stress-coping model, they investigated adjustment among the chronically ill using six different coping strategies. Neither level of disability nor any other distinction among illnesses played a role in determining which coping strategies were effective in promoting adjustment to illness. However, responses to open-ended questions by patients with cancer and rheumatoid arthritis suggested that illness related disabilities did affect psychosocial adjustment. These qualitative findings suggested that possibly quantitative instruments may not have been sensitive to disease impact and disability.

Psychosocial adjustment to illness and its relationship to type and severity of illness, cognitive appraisal

(meaning of illness) and family function were studied by Arpin, Fitch, Browne and Corey (1990). In a study of 216 oncology, rheumatology and gastroenterology patients, the cognitive appraisal or meaning variables exceeded the importance of all other variables in explaining 14% of a person's adjustment to illness. While 70% of this sample reported good adjustment to illness, degree of disability was positively related to perception of disability ($\underline{b}$ = 5.80). These findings may have reflected a sampling bias in this study in favor of patients with minimal limitation in physical functioning as only the patients with oncology diagnoses appeared to have relatively chronic conditions.

Pollock, (1986) investigated physiological and psychological adaptation to chronic illness while hypothesizing that individuals with a hardiness characteristic would have more adaptive behavior than individuals without the characteristic. Studying individuals with rheumatoid arthritis, diabetes and hypertension, Pollock found that presence of the hardiness characteristic was significantly correlated (r = .43) with physiological adaptation and (r = .62) with psychosocial adaptation in the

diabetic group but not for the hypertensive or rheumatoid arthritic groups. Generalizations about chronic illness in this study could not be made when recognizing that differences in etiology, symptoms and treatment may present diverse stressors for patients' adaptive abilities.

Physiological and psychological adaptation to chronic illness was studied using the Adaptation model in 211 patients (Pollock, Christian and Sands 1990). The personality characteristic of hardiness was the only variable significantly related to both psychological ($r = -.13$, $p = <.05$) and physiologic ($r = -.16$, $p = <.01$) adaptation. Physiological adaptation was significantly different among three chronic illness categories (rheumatoid arthritis, multiple sclerosis and hypertension). Findings suggested that physiologic adaptation may be disease specific and multi-variable comparisons may leave many questions unanswered.

The influence of physical health status, stressful life events and various moderator variable on psychosocial adjustment in a chronically ill (MS) population was studied by Zeldow and Pavlou (1984). Physical dysfunction as measured by the SIP had a pervasive influence on personal

and interpersonal functioning. Mean physical impact scores were higher (24.6) than psychosocial impact scores (17.4) and overall impact 21.1 falling in the middle. Using combined indicators of personality and psychosocial adjustment, the authors concluded that greater physical disability is associated with decrements in personal efficiency and well-being, adaptive autonomy, self-reliance, social confidence and actual social contacts.

Examination of the relationship of stress appraisal and coping responses to multiple behavioral indices of illness adjustment among 101 patients with diverse chronic conditions was studied by Bombardier, D'Amico and Jordan (1990). Variables studied included functional impairment, depression, symptom severity and coping. Patients indicated greater psychosocial dysfunction (29.2) than physical impact (17.6) as rated by the SIP. Using regression analysis, emotion-focused coping was positively related to poor psychosocial adjustment ($r = .28$) and depression ($r = .29$) after controlling for rated disease severity. Appraisal of illness as limiting one's ability predicted greater emotion-focused coping responses ($r = .38$) and poorer adjustment to illness. Use of negative coping strategies predicted

negative adjustment. Illness stress and functional impairment were measured by the SIP. The authors concluded that specific types of illness appraisal and coping responses were concurrent predictors of illness-related adaptive functioning, depression and, to a lesser extent perceived symptom severity.

A longitudinal study of 103 individuals with multiple sclerosis (M.S.) looked at self concept measurement differences (t2-t1) as an indicator of adjustment to disease (Brooks and Matson, 1982). No change was found in patient self concept over time was found during this study. However when compared to a non-M.S. comparison group, the study group had a small but significantly different change in self concept (t-3.09 ($p < .01$). In this study, change in mobility (disease severity) did not correlate significantly with change in self concept.

A 1994 review of research on psychosocial adjustment to neuromuscular disorders by Liveenh & Antonak, confirms the paucity of research in this area specific to individuals with PD. The authors conclude that numerous clinical and empirical investigations have studied the occurrence and nature of depression among people with Parkinson's Disease,

however little research has been directed at exploring other psychosocial reactions to this disease (Livneh & Antonak, 1994).

Patterns of adaptation to PD were studied in 44 patients by Dakof and Mendelshon (1989). Patients participated in interviews and completed the Symptom Checklist 90. A Q-sort technique was used to analyze the interview data. Four clusters of adaptation evolved; sanguine and engaged (Cluster I), depressed and apprehensive (Cluster II), depressed, ashamed and misunderstood (Cluster III) and passive and resigned (Cluster IV). Disease severity, but not demographic or other health variables, discriminated the groups. Patients with mild to moderate impairment adjusted effectively to their illness (Cluster I). Clusters III and IV seemed primarily a function of physical condition.

Summary

The literature discussed here supports the assumption that chronic illnesses act as life stressors and that coping may be a mediator in overall adjustment. The relationship of disease severity to adjustment and the role of disease impact as a stressor warrants further study. Studies in

movement related diagnoses and in PD in specific revealed a variety of interpretations of this relationship. Diversity in the selection of variables and in their operationalization limits comparison to PD. A majority of studies provided support for the existence of considerable psychosocial impact from PD and from other movement related diseases. The studies reviewed highlight the need and importance of disease specific reliable and valid instruments in clinical studies.

The majority of studies were discriminative in nature rather than evaluative. However, cross-sectional data limits the applicability of findings especially where degenerative neurologic diseases are concerned. The need for evaluative studies is critical to understanding the impact of illness overtime, the effect of interventions and their relationship to overall adjustment.

CHAPTER III

Methodology

Chapter III describes the research design, sample, instrumentation, data collection and analysis procedures which were used in this study.

Research Design

This study was done in parallel with a primary double blind placebo controlled pharmaceutical clinical trial which was conducted to determine the safety and efficacy of three doses of tolcapone when compared to placebo (inactive substance) for the treatment of individuals with Parkinson's Disease. A nonequivalent control group (naturally assembled, ambulatory out-patients) design was used for the both studies (Campbell & Stanley, 1963). The focus of this parallel study was to determine if patients participating in the primary study who were treated with tolcapone experienced improved psychosocial adjustment to illness and experienced less impact of illness (PD) than patients treated with placebo.

Using the criteria detailed by Campbell and Stanley (1963), the study's design was analyzed for threats to internal and external validity. Internal validity is the basic minimum without which any experiment is uninterpretable: did in fact the experimental treatment make a difference? In this study all eight threats to internal validity, history, maturation, testing, instrumentation, regression, selection, mortality and interation of selection, maturation etc. were controlled by the experimental design. The process of random assignment controlled for the threats to representativeness or achieving pre-treatment equality of groups. External validity asks the question of generalizability. Lack of random selection and the small sample size in this study limited the generalizability of the findings.

Sample

The target population was composed of individuals diagnosed with idiopathic Parkinson's Disease being seen at an outpatient movement disorder clinic. Only individuals who met the inclusion and exclusion criteria for participation in the primary study were invited to participate in this study (see appendix A).

Participants for this study included a sample of 46 individuals with idiopathic Parkinson's Disease who met the criteria for participation in the primary study. There were a total of 49 sets of responses (pre and post treatment questionnaires) with 46 final usable data sets.

The final total study sample was comprised of 19 females (41%) and 27 (59%) males with a mean age of 64 (range 40-79). Of the 46 subjects, 5(12%) were employed and 41 (87%) were retired. The majority or 43 (90%) were married. A total of 2 (6%) were divorced or separated and 1 (4%) was widowed. Educational level reflected a mean of 13 years of education. Eleven (23%) had high school educations, 18 (34%) had graduated from college and 10 (21%) had received graduate or professional education. The mean duration of PD was 10.25 years (range of 2.3 to 20.3).

Random assignment to treatment groups was determined and conducted prior to the first patient enrollment by the sponsor of the primary study. Dose-related treatment groups were utilized to meet sampling needs for the primary study. Homogeneity across groups was confirmed prior to data analyses and is discussed in Chapter 4. Demographic characteristics of the subjects by treatment group are

illustrated in Table 1. Under blinded conditions, ten patients each were assigned to the 50 and 400mg groups, 12 to the 200mg group and 14 to the placebo group. Age across treatment groups ranged from a low of 62 in the placebo group to a high of 67 in the 400mg group. Duration of PD was lowest in the placebo group, 8 years, to a high of 12 in the 50mg group. Unified Parkinson's Disease Rating Scale (UPDRS) score for motor function ranged from a low of 32 in the 400mg group to a high of 39 in the 50mg group. A total UPDRS score low of 37 was noted in the 400mg group to a high of 47 in the placebo group. Disease staging as measured by the Hoehn/Yahr was the same, 2, across all treatment groups.

Projective statistical techniques were used to determine what size samples would be needed to detect the same changes as were found in this study. These calculations suggested that if all participants in the multi-center study (n = 152) had participated in this study, significant differences at the p = .05 level might have been detected.

Despite the advantages provided by the experimental design, the findings of this study are limited because of the small sample size. The samples for each treatment group did not reach those projected by the a-priori power analysis

Table 1

Sample Description by Treatment Group

Characteristic-	Placebo	Tolocapone 50mg	Tolocapone 200mg	Tolocapone 400mg
n	14	10	12	10
Age	62	64	64	67
PD Duration	8	12	9	11
Motor UPDRS*	38	39	35	32
Total UPDRS*	47	46	45	37
Hoehn/Yahr*	2	2	2	2

*Disease severity determinant

calculations. This limits the findings from three perspectives: a) small treatment group sizes minimize the possibility for detection of significant differences between groups and b) limits the generalizability of the study's overall findings and c) the possibility of variability in such small cell sizes could obscure any real differences between groups.

Instrumentation

The following sections describe the instruments used in the study. Representative items from each data collection instrument are presented in the Appendices.

Sickness Impact Profile (SIP)

The Sickness Impact Profile (see Appendix B) is composed of 136 items describing specific health related dysfunction behaviors. Respondents check only items describing dysfunction due to their illness. The purpose of the instrument is to provide a behaviorally-based measure of health status or illness impact (Bergner, 1977). The SIP results reflect a subject's perception of performance of those activities associated with daily life activities. The instrument is composed of two dimensions, physical (3 subscales) and psychosocial (4 subscales), and five

independent categories for a total of 12 subscales. In this study the SIP results were computed using an overall total illness impact score, (the sum of all subscales), a physical dimension score (the sum of the ambulation, mobility and body care and movement subscales), a psychosocial dimension score (the sum of the emotional behavior, social interaction, alertness and communication subscales), and 5 individual independent category scores (the work, sleep and rest, eating, home management and recreation and pastimes subscales).

The SIP has been tested extensively in many diagnostic categories for test-rest reliability ($\underline{r}$ = 0.92) and internal consistency reliability ($\underline{r}$ = 0.94). Results are well above the .80 acceptable limit for interviewer-administered and self-administered instruments (Nunnally, 1978). Convergent and discriminant validity have been evaluated using the multi-trait multi-method techniques. A summary of the multitrait-multimethod correlations of overall scores of the SIP with the SAD (self-assessment of dysfunction), SAS (self assessment of sickness), and the NHIS (National Health Interview Survey Index of Activity Limitation) were 0.92, 0.82, 0.86 and 0.85 respectively (Bergner, 1981).

A cross sectional study by Longstreth et al. (1992) was performed to determine the utility of the SIP with PD patients. The overall SIP score, the physical dimension and psychosocial dimensions were significantly correlated (p <.001) with the gold standard PD disability measures (Hoehn and Yahr [see Appendix E] and the Columbia Scale).

In this study the SIP Cronbach's alpha coefficient was 0.89 for the entire instrument. Subscale alpha's ranged from 0.86 to 0.87. Prior to the experimental, intervention the SIP total score correlated with the disability measures (baseline motor UPDRS score), (r = .45, p = .001), and with the total UPDRS (r = .55, p = .0001). The SIP also was correlated with the Hoehn and Yahr (r = .42, p = .003). These findings were similar to Longstreth's (1992) suggesting a relationship between motor function and disease severity.

Psychosocial Adjustment to Illness-SR (PAIS-SR)

The PAIS-SR (see appendix C) is a self report instrument designed to assess the quality of a patient's psychosocial adjustment to a current medical illness (Derogatis, 1978). This 46 item Likert type instrument has been used extensively in psychological, sociological and

clinical medical settings (Derogatis,1990). The seven subscales of the PAIS-SR were developed through a combination of rational-deductive and empirical-analytic techniques. Internal consistency testing of the PAIS-SR was assessed in three chronic illness populations: dialysis, lung cancer and cardiac patients. Cronbach's alpha coefficients for the dialysis population ranged from 0.63-0.80, in the cancer patients the range was from 0.12-0.93 and in the cardiac population from 0.47 to 0.85. The subscale which included the item with the .12 score has been revised.

Construct validation and principal components analysis provided support for the seven theorized dimensions using a cancer cohort of 120 patients. The PAIS-SR was tested for convergent validity in comparison with four like measures of psychological distress: the Affect Balance Scale (ABS), SCL-90-R General Severity Index, and the Patient's Attitudes, Information and Expectancies Scale (PAIE). PAIS-SR total score correlated with the GAIS (r = .81), SCL-90 (r = .60), ABS (r = .69) and PAIE (r = .64).

Internal consistency estimations for the PAIS-SR in this study were 0.80 for the total instrument with subscale alphas ranging from 0.75 to 0.81.

Unified Parkinson's Disease Rating Scale (UPDRS)

The UPDRS (see Appendix D) is a clinical evaluation method commonly used by movement disorder specialists to objectively assess an individuals symptoms of Parkinson's Disease (Fahn & Elton, 1987). The instrument contains three dimensions: 1) mood, 2) ADL (activities of daily living), and 3) motor. In this study the motor UPDRS scores were used. The motor score reported is in the "off" condition. This score was determined by physical examination on day 1 (prior to) and on day 42, at the conclusion of treatment with tolcapone (endpoint). The "off" condition is defined as motor function without the benefit of levodopa treatment and is considered the best approximation of improvement over time. Sample items from the UPDRS appear in Appendix B. Reliability and validity were not published at the time of development, however a post hoc assessment was performed by van Hilten, van der Zwan, Zwinderman and Roos, 1994. Reliability estimates of 0.88 for the total score and concurrent validity of $\underline{r}$ = 0.75 when compared with the Hoehn

and Yahr were reported (van Hilten, van der Zwan, Zwindermkan and Roos, 1994). The UPDRS is considered the "gold standard" by movement disorder specialist for determining motor function in individuals with PD in clinical and research settings.

Hoehn and Yahr

The Hoehn and Yahr (see Appendix E) is a 5 point scale used to categorize a patient's disease stage. Hoehn and Yahr data were collected in order to analyze subgroup differences by disease stage and to determine if patients disease stage was acceptable for initial eligibility for the primary study.

Demographic Questionnaire

An investigator-developed demographic questionnaire was used to collect representative demographic data (see Appendix F). These data were used to describe the sample as well as to allow for analysis of specific subsets within the sample and potential correlations with outcome variables. Representative demographic data included age, sex, education, marital status, and number of years with PD.

Data Collection

Approval to conduct the research was obtained from the Research Committee at the University-affiliated movement disorder clinic where patients were recruited, and from the Committee for the Protection of Human Subjects (CPHS) at the University of San Diego (see Appendix G). After permission was obtained from the appropriate institutions, chart abstraction was used to gather information to determine preliminary subject eligibility. Patients meeting the criteria for inclusion were approached to determine their interest in participation (see Appendix A). Individuals received a complete explanation of the project including assurance of confidentiality and anonymity. Individuals who agreed to participate, provided informed consent and who met the inclusion and exclusion criteria were scheduled for a preliminary screening visit.

Qualified and consenting subjects came to the clinic for disease severity determination and rating of motor symptoms by a physician specially trained in movement disorders. Patients who met the primary study inclusion criteria and who provided informed consent were approached for participation in the nursing study. At the screening

visit for the primary study, all participants had a complete physical and neurologic exam, safety laboratory tests, an EKG, and urinalysis. Participants were also instructed in how to complete a diary of their Parkinson symptoms. Participants whose screening exams were normal returned in 2 weeks for a baseline visit for the primary study. At the baseline visit, all nursing study participants completed the nursing study instrument packet, prior to beginning treatment with the investigational medication. Participants began treatment on the day following the baseline visit with one of the three double blind doses of study medication or placebo. Participant experimental group assignment had been pre-randomized by the primary study sponsor. Study participants were followed over six required primary study visits for safety and monitoring purposes. On the final visit of the primary study, day 42, all nursing study participants completed a second set of nursing study instruments identical to those completed at the baseline visit.

Data Analysis

Descriptive statistics were used to characterize the sample and distribution characteristics. Measures of

variability were calculated on the control and treatment groups to determine the homogeneity of the treatment groups in order to meet statistical test assumptions. Non-parametric statistical techniques were used for comparison of subgroup distributions within the sample because of the nominal level of the data (Kerlinger, 1989).

Pearson's Product Moment Correlation coefficients were calculated to determine relationships between demographic and study variables.

The research hypotheses were tested using repeated measures analysis of variance and planned comparisons (Munro, Visantainer & Page, 1986). Assumption requirements of homogeneity of variance, equality of covariance matrices and compound symmetry were satisfied prior to analyses. Following preliminary hypothesis testing, further post-hoc analysis were performed where indicated.

The statistical tests were selected based on the assumptions of homogeneity of variance (the groups should have equal variances), mutual exclusivity (the groups are independent of each other) and compound symmetry. There are two components of compound symmetry; the correlations across the measurements are the same, and that the variances should

be equal across measurements (Munro et al., 1986). The assumptions of the repeated measures analysis of variance were all met prior to the analyses.

Summary

This chapter has detailed the methods used in the study. An experimental design was used to test the hypotheses in this study. It was hypothesized that impact of illness and psychosocial adjustment would improve after treatment with tolcapone. A naturally existing sample of individuals with idiopathic Parkinson's Disease were randomly assigned to one of four treatment conditions of a double-blind placebo controlled primary study of tolcapone. Repeated measures analysis of variance was used to test hypotheses posed for this study. Post-hoc analysis was also performed to insure treatment group homogeneity.

CHAPTER IV

RESULTS

Study findings are presented in this chapter. The chapter includes the following sections: 1) data reduction, 2) determination of homogeneity of treatment groups, 3) hypothesis testing, and 4) post-hoc analyses.

Data Reduction

Data reduction was accomplished through a plan of data cleaning. Prior to data entry procedures, all study instruments were scrutinized for missing data and unacceptable data which were defined as data out of range of study variable limits. Initially 49 sets or partial sets (pre and post questionnaires) were considered for inclusion. Following extensive cleaning and data verification, 46 complete sets of data were used for analysis with the SIP, PAIS-SR, demographic data and functional status measurements.

Determination of Homogeneity of Treatment Groups

Homogeneity of treatment groups was determined using analysis of variance procedures on all demographic and treatment variables. In this double blind design, all subjects received treatment (placebo included), therefore all groups were included in analyses. No significant differences were found between demographic or treatment variables when comparisons by treatment group were examined. Post-hcc analyses using Scheffe's test and Bonferroni (Dunn) T tests confirmed that no significant differences existed between members of any of the treatment groups (Munro, Visantainter & Page, 1986).

Hypotheses Testing

Repeated measures analysis of variance planned comparisons were performed to test the study hypotheses. Tests of the assumptions of multivariate normality, equality of covariance and compound symmetry were met for each of the hypotheses prior to performing the analyses (Munro et al., 1986). Table 2 summarizes the results of hypotheses testing. Using repeated measures analyses, significant differences were detected when combined dose-related treatment groups were compared to the placebo group for each of the three

Table 2

Results of Hypotheses Testing

	SS	DF	MS	F	P
Illness Impact	303.138	1	303.138	10.024	<.003
	1207.071	42	30.240		
Physical Impact	246.279	1	246.279	10.958	<.002
	943.922	42	22.474		
Psychosocial Impact	349.042	1	349.042	8.177	<.007
	1792.042	42	42.684		
Adjustment	9758.970	1	9758.970	2.356	<.132
	173972.828	42	4142.210		

illness impact hypotheses. These groups were conbined due to the small number of subjects per group, and to specifically test the hypotheses generated for the study.

Hypothesis 1, Patients receiving tolcapone experienced significantly less total illness impact (p = <.003) when compared to patients receiving placebo.

Hypothesis 2, Patients receiving tolcapone experienced significantly less physical illness impact (p = <.002) when compared to patients receiving placebo.

Hypothesis 3, Patients receiving tolcapone experienced significantly less psychosocial illness impact (p= <.007) when compared to patients receiving placebo.

Hypothesis 4, Psychosocial adjustment to illness was improved in all patients after treatment with tolcapone but did not differ significantly from patients receiving a placebo.

Post-Hoc Analyses

Individual variable score change from baseline to week six (day 42) was used to compute the differences in SIP and PAIS-SR scores for subjects in the placebo group and treatment groups.

Post-hoc analyses were performed to determine if any significant pairwise comparisons of individual treatment groups could be found. When the changes in scores from baseline to endpoint were compared no significant differences were found. However, when the percent change was tested using a Bonferroi (Dunn) T, a significant ($p = <.05$) change from baseline to endpoint was found between the 200mg tolcapone and placebo groups.

Though the changes in illness impact and psychosocial adjustment from baseline to endpoint were not statistically different by individual treatment group, the importance in the changes noted may be more clinically than statistically relevant. Figures 1, 2, and 3 illustrate the changes found in illness impact. The importance of clinical significance is discussed in Chapter 5.

Reductions in illness impact were found in all three tolcapone dose treatment groups in total illness impact (SIP) scores, physical dimension scores and psychosocial dimension scores. In contrast, patients in the placebo group reported increases (worsening) in illness impact over the same 6 week period. Table 3 illustrates the pre- to post-scores. Though none of these changes were found to be

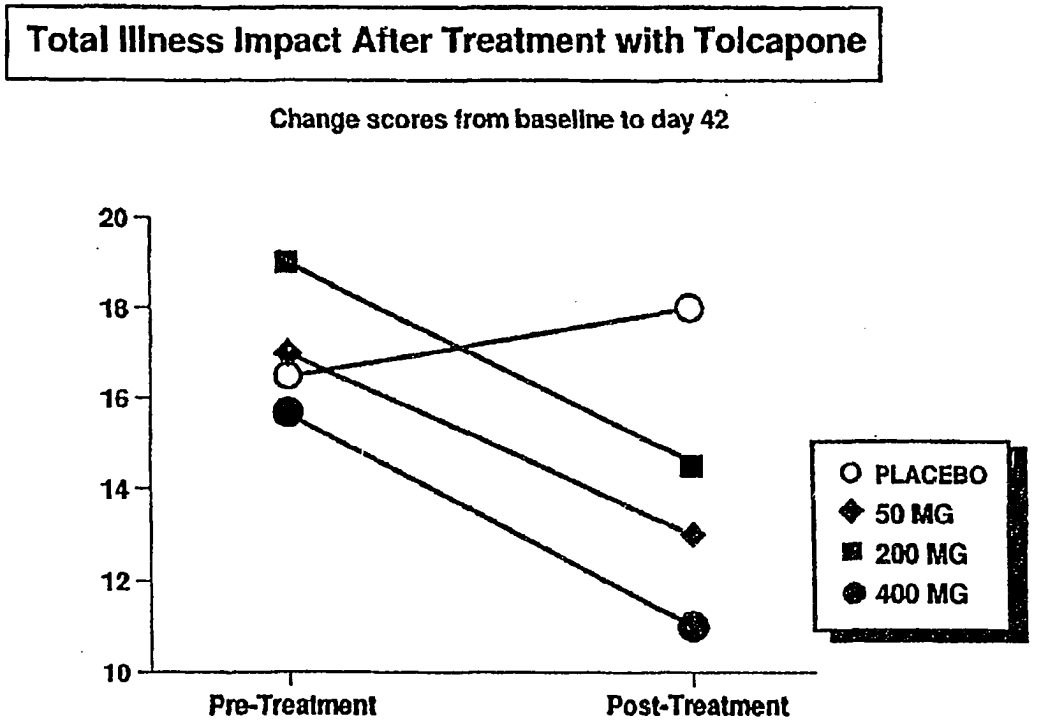

Figure 1: Total Illness Impact After Treatment with Tolcapone

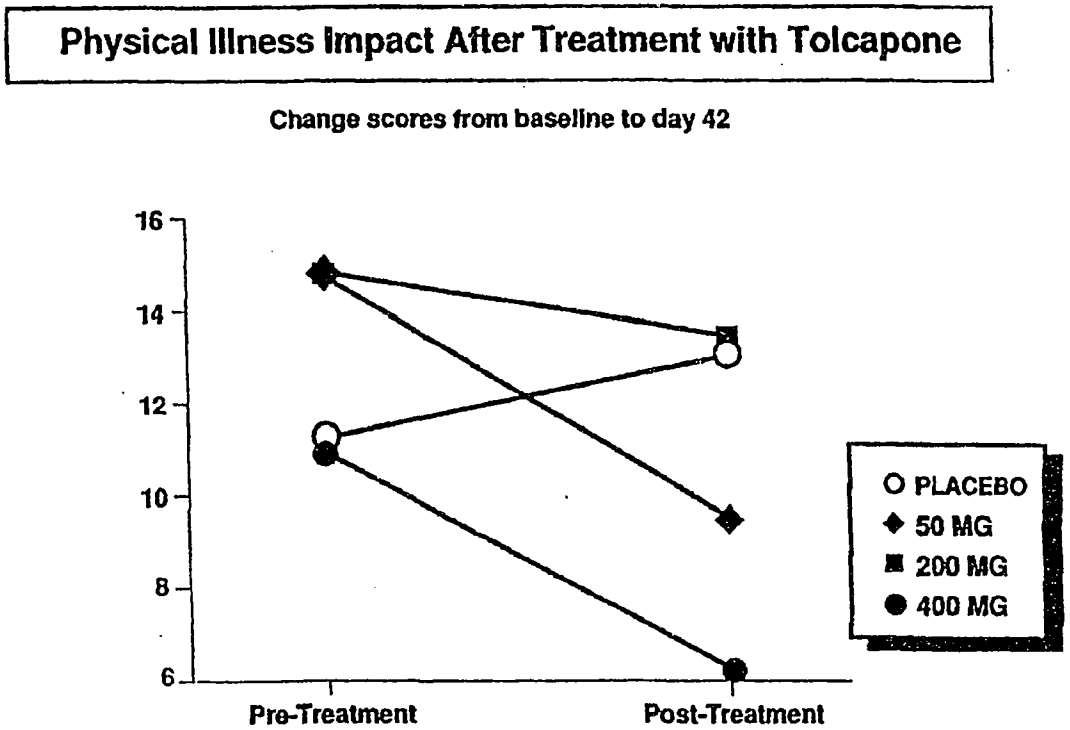

Figure 2: Physical Illness Impact After Treatment with Tolcapone

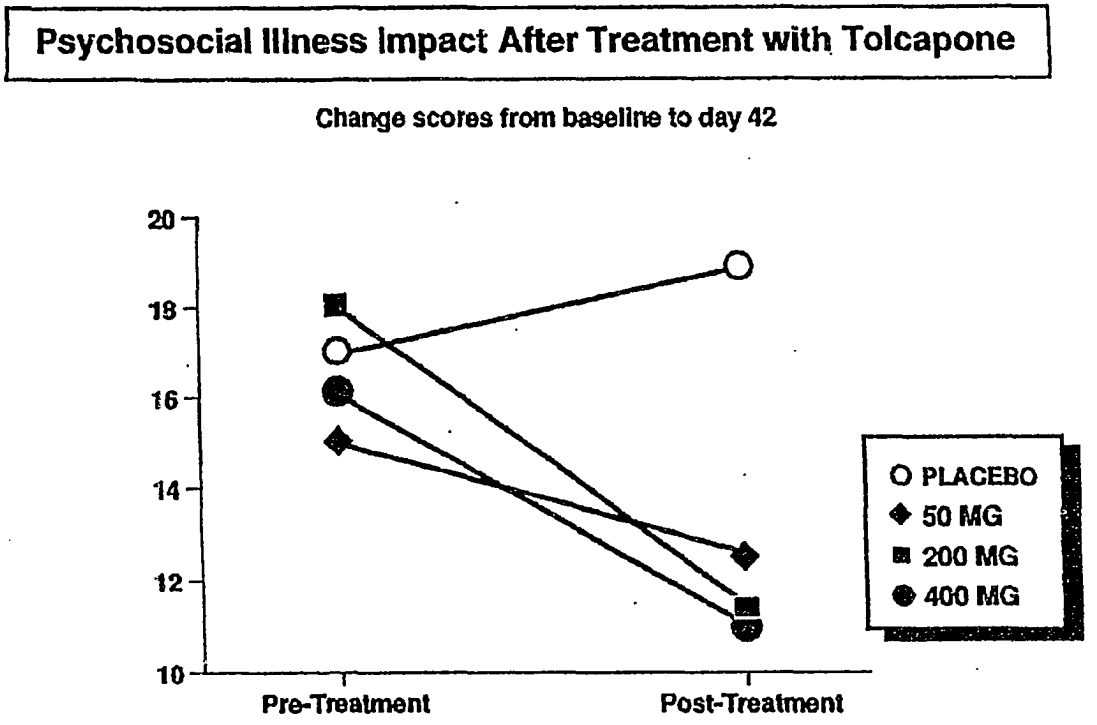

Figure 3: Psychosocial Illness Impact After Treatment with Tolcapone

Table 3

Dose Related Illness Impact Pre/Post Treatment

	Placebo		50mg		Tolcapone 200mg		400mg	
n	14		10		12		10	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Total SIP	16.8	18.0	17.0	13.7	19.1	14.6	15.9	10.2
Physical	11.6	13.2	15.0	9.7	15.1	13.5	10.8	6.1
Psychosocial	17.5	18.7	14.9	12.4	18.0	11.4	16.0	10.7

statistically significant by treatment group, all of the treatment groups reported they experienced less clinical illness impact. Similarly in all of the tolcapone treatment groups, the 12 individual category scores of illness impact (total scores) patients reported improvement (lowering of illness impact scores) in all categories with the exception of 2. In the 50mg tolcapone group no change was reported (0.0) between baseline and 6 weeks. Similarly, the 200mg tolcapone group reported a 2.2 change (worsening) in mobility from baseline to week 6.

In the placebo group 8 category scores increased (worsening of illness impact) while 3 reported improving and 1 score with no change (0.0). Patients receiving placebo reported a (-0.2) change in emotional behavior, a (-5.2) change in communication, and a (-6.8) change in recreation. The raw change and percent change scores are illustrated in Table 4.

Similarly, though no significant differences were found in psychosocial adjustment to illness, many dose related response improvements were observed in a subscale analyses of the PAIS-SR. In the total sample post-treatment improvement was found in a majority of the subscales and in

Table 4

Illness Impact Change From Baseline to Endpoint

	Placebo	50mg	200mg	400mg
Score Change Raw (%)				
Illness Impact	+1.2(7%)	-3.3(20%)	-4.5(23%)	-5.7(36%)
Physical	+1.5(13%)	-5.4(36%)	-1.6(11%)	-4.6(43%)
Psychosocial	+1.2(7%)	-2.6(17%)	-6.6(37%)	-5.4(34%)
Adjustment	-.6(<1%)	-16(5%)	-12(3%)	-20(6%)
UPDRS motor	+0.8(2%)	-1.1(2%)	-3.5(8%)	-3.2(8%)

the PAIS-SR total score (Table 5). In the 200mg Tolcapone group, all subscale and total scores were improved. In the 50mg and 400mg groups, small negative changes (+.1 and +.2) were found respectfully in the extended family relationship subscale. The 50mg group also reported a (+.5) worsening in psychological distress. In contrast the placebo group reported psychosocial adjustment worsened in the sexual relationship (+1.28) and social environment (+.61) subscales. However, placebo patients reported improvement in orientation to healthcare environment (-.43), vocational environment (-.57), domestic environment (-.93) and extended family relationships (-.14). Total PAIS-SR scores improved by (-.64). Though many of the improvements in illness impact and psychosocial adjustment were not statistically significant, the importance of these findings appeared to be in the realm of clinical significance.

At baseline, indicators of association were found between the impact of illness (SIP) and disease severtiy. Similar correlations were not found between the PAIS-SR and disease severity. Table 6 describes the associations found at baseline and correlations of change found at endpoint.

Table 5

Dose Related Psychosocial Adjustment Responses

	Placebo		50mg		200mg		400mg	
n	14		10		12		10	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
HCSUB	6.0	-5.6	4.9	3.7	7.0	6.1	5.1	3.4
VESUB	6.4	-5.1	7.4	6.2	5.6	2.9	5.5	5.2
DESUB	7.6	-6.7	7.2	5.3	7.9	7.3	4.9	4.5
FRSUB	2.4	-2.5	1.2	1.3	3.0	2.4	.9	1.1
SRSUB	4.3	5.0	3.1	3.1	5.8	5.1	5.4	5.1
SESUB	6.9	7.5	7.6	6.2	6.8	6.5	5.3	3.8
PDSUB	5.3	5.7	6.4	6.9	6.0	4.6	8.0	5.9
RAW	357	356	354	337	364	352	345	325

HCSUB-Healthcare orientation VESUB-Vocational Environment
DESUB-Domestic environment FRSUB-Extended Family Relationship
SRSUB-Sexual Relaitonships SESUB-Social Environment
PDSUB-Psychological Distress RAW- Total Adjustment Score

Table 6

Post Hoc Comparison

	UPDRS Total		Motor UPDRS		Hoehn & Yahr
	Pre	Post	Pre	Post	Pre Post
SIP TOTAL	.55***				

At endpoint, minimal correlations of change were found between disease severity and illness impact (r = .25, p = <.08), and SIP psychosocial dimension (r = .26, p = <.08) suggesting the relationship between disease severity and illness impact may have been independent of the treatment.

Summary

This chapter has summarized the methods used to accomplish data reduction and confirm homogeneity of treatment groups. Correlations between demographic and study variables and hypotheses testing and results were discussed. The impact of illness was lessened in individuals treated with tolcapone. When compared with improvement in motor function, illness impact percent change appeared to be more responsive to treatment. Psychosocial adjustment though improved in individuals treated with tolcapone appeared to be a less robust response than illness impact.

CHAPTER V

DISCUSSION AND RECOMMENDATIONS

This chapter presents a discussion of the findings of the study, the strengths and limitations of the study, and recommendations for future research. The study's findings are compared and contrasted to previous research reported in the literature.

Illness Impact

The patient's perspective of the impact of Parkinson's Disease on overall quality of life has been a major focus of this study. Illness impact emerged as the most robust variable. Pre to post treatment changes in total illness impact, physical impact and psychosocial impact scores primarily followed a treatment response pattern (placebo patients worsened, and treatment patients improved) over the length of the study.

Baseline illness impact scores for total impact, physical impact and psychosocial impact were (17.29), (13.10) and (16.78) respectfully. These were somewhat

different from those of Busenbark et al.'s (1991)study of PD patients. Busenbark's (1991) sample appeared to experience more illness impact than this sample with total scores of (19.0), physical dimension scores of (17.1), and psychosocial dimension scores of (20.2). In contrast, Zeldow and Pavlou's (1988) MS sample had higher physical impact scores, (22.3)lower psychosocial impact scores, (14.0) and more similar in total impact (19.2) when compared to this study sample. Deyo et al.'s (1982) study of Rheumatoid Arthritis (RA) patients rated total impact (15.6), physical impact (14.0) and psychosocial impact (11.3) indicating the RA patients felt less illness impact than the PD patients in this study.

Sano et al. (1990), in a study of PD dementia, reported the only evaluative use of the variable of illness impact in a movement disorder related sample. They reported significantly ($p < .05$) more subjects categorized as improved on the SIP score in the treatment group compared to the placebo group however no actual data for this conclusion was published (Sano et al.,1990). Significant improvement was reported in the drug treatment group compared to the placebo group on the rating of recreation and pastime. Again no

actual data were published. The present study's findings had similarities to those reported by Sano, et al. (1990). Total illness impact improved across all treatment groups when compared to the placebo, as did the recreation and pastime subscale scores in the three treatment arms. However, in this study, the recreation and pastime subscale in the placebo group actually reported improvement by (+ 6.75). Such a change can only be accounted for by a "placebo" effect since all of the other placebo group scores increased (worsened) during the study, with the exception of very small changes in the emotional behavior subscale (10.66 pre, 10.46 post) and work subscale (43.16 pre and 43.13 post). Comparisons with Sano et al.'s (1990) study must be done with caution. Raw data were not reported and therefore actual comparisons of methods/analysis could not be done with precision.

When comparing the published SIP scores of related samples, and of studies with PD patients, the PD sample in this study appeared to be consistent with existing literature with respect to the variability in disease severity among individuals with PD. The motor scores of patients in this study were compared on the basis of the

worst "off" of the day (approximately 8-10 hours without medication). All patients were evaluated under the same conditions in order to control for between patient variability. This element of control is not usually found in cross-sectional studies and therefore provides a higher level of precision of measurement.

Disease Severity and Illness Impact

The relationship between disease severity and illness impact was explored using bivariate correlations. Ratings of disease severity at baseline (UPDRS total and motor and Hoehn and Yahr) indicated that all three measures were associated with many components of illness impact. Since Parkinson's Disease is progressive in nature, disease staging indicators (Hoehn and Yahr) could be expected to be associated with indicators of illness stress. This study's findings like those of Zeldow & Pavlou (1988) revealed that severity of illness (not duration) was a more influential determinant of a patients perception of impact of illness. Duration of PD was only mildly correlated with emotional behavior and home management.

The findings of this study were similar to those of Brown and MacCarthy's study of PD who found significant

associations of illness stress and patient self report of best/worst disease severity (r = .54, p = <.001, r = .52, p = <.001).

In contrast, in Kurlan et al.'s study (1989) the SIP total correlated significantly (r = .32, p <0.5) with age and more closely with duration of PD (r = .41 p = <.01) and Hoehn/Yahr (r = 0.42, p = <0.2). Comparable findings in this study support Kurlans' data on the relationship of disease severity and the SIP total (motor UPDRS and Hoehn/Yahr both significantly correlated (p = <.001 and p = <.003) respectfully. However they differ in that age did not correlate with illness impact in this study as it did in Kurlan, et al.'s (1989) study.

Busenbark, et al.'s (1991) study published no data of correlations of SIP with disease severity, however they did report that PD patients scored significantly higher than ET patients in total SIP, physical dimension and psychosocial dimension scores.

In this study, the change in motor UPDRS (from baseline to endpoint) was only mildly correlated with the change in SIP total (r = .26, p = <.09) and the change in SIP psychosocial score (r =.26, p = <.08). These findings

suggested that although motor function was improved by treatment with tolcapone, the changes in illness impact appeared to be independent of changes in motor function.

Psychosocial Adjustment and Disease Severity

At baseline, disease severity was not as strongly associated with psychosocial adjustment as was impact of illness. Motor UPDRS was associated with only 2 PAIS subscales, domestic environment (r = 25, p = <.09) and sexual relationships (r = .43, p = <.003). Total UPDRS was associated with the same subscales domestic environment (r = .33, p = 0.02) and sexual relationships (r = .45, p = <.002). In addition there was also an association with social environment (r = .30, p = <.04). The psychological distress subscale and PAIS-SR total score were related to duration of PD, motor UPDRS at baseline, total UPDRS at baseline and Hoehn/Yahr. Duration of PD at baseline was not correlated with any of the subscale or total PAIS-SR measures. These findings are similar to those of MacCarthy and Brown, (1989) whose adjustment measure of depression was associated with disease severity (r = .37, p = <.001 and acceptance of illness (r= .55, p = <.001). Functional disability (as measured by ADL) proved to be the index which

best predicted depression in MacCarthy's study of PD patient's.

These findings supported those of previous studies (MacCarthy & Brown, 1989, Viney & Westbrook, 1984) which suggested that adjustment to chronic illness may be more closely related to appraisal of illness and intervening variables than disease severity or duration alone. Larger evaluative studies of PD such as this one, would aid in clarifying these preliminary findings.

Illness Impact and Psychosocial Adjustment

The impact of illness as a stressor in Parkinson's Disease has been supported by this study's findings. All three hypotheses of the effect of tolcapone on decreasing illness impact were supported. The relationship of decreased illness impact as a contributor to psychosocial adjustment remains unclear. The relationship of change in illness impact and change in psychosocial adjustment is also unclear. The significant change over time of selected illness impact variables and their association with adjustment suggests the need for future studies with larger samples sizes and similar control measures. Change in psychosocial adjustment was associated with change in SIP

total score (r = .25, p = <.11). This nonsignificant association only mildly supports the relationship found at baseline (r = .72, p = <.0001). Further studies are needed to fully understand the nature of this relationship.

Clinical Significance

Previous evaluative studies in PD have primarily focused on physiologic or disease state outcome measures. The importance of these studies rests more on clinical significance. Physiologic or disease state measurement provides information to clinicians but are of limited interest to patients and may often correlate poorly with functional capactiy or perceived well being (Guyatt, Feeny, & Patrick, 1993). The key to clinical significance lies in interpretability, whether a particular change in score represents a trivial, small but important, moderate or large improvement, or deterioration.

In this study, changes in illness impact and disease state were standardized into percent change scores in order to enhance interpretability. Using statistical techniques (t-tests) only 1 of 20 pairwise comparison's were significant (total illness impact in the 400mg group compared to placebo). However, using the standardized

percent change comparisons, nine of nine illness impact by treatment group comparisons showed improvment (11% to 43%). In comparison the traditional disease severity percent changes showed improvement however considerably smaller than the quality of life variables (2% to 8%). Such differences suggested that traditional disease severity assessments, however informative for treatment considerations, may not correlate well with patients perception of functional capacity or well being.

Implications and Recommendations

The importance of subjective patient centered measurement of disease symptoms and experience has yet to be recognized in all areas of neuroscience practice. Findings from studies such as this highlight the need for incorporation of this critical component into clinical practice.

The evaluative methods used in this study provide a new level of knowledge compared to previous cross sectional studies. Interpretation and application of findings must be cautious, however, because of the small sample size. However power analysis estimation using the treatment differences found in this study, project that significant differences at

the .05 and .03 levels could be detected if this study were replicated with larger sample size studies. Despite the importance of generalizability of findings, it should not be overlooked that, when examining differences in clinical status and function, the importance of small if not significant changes should be considered.

In the out patient setting, improvement and change is often measured objectively, by the clinician. Determination of improvement may be based not on significant benefit from therapy, but by lack of adverse effects or deterioration from a previous assessment. Previous studies have examined disease state alone without inclusion of subjective or quality of life outcome measures. The importance of subjective outcome measures is particularly important when considering outcome in the geriatric age group such as Parkinson's disease. Elderly patients often suffer from ongoing disabilities which confound their illness experience.

It is obvious that quality of life can be significantly affected by PD and the drugs employed to treat it (Koller, 1994). A concern has been raised that these (quality of life) instruments may not have the sensitivity to detect

changes in quality of life compared with the more traditional measures of clinical status (Koller, 1994). Two important points should be raised: quality of life measures may include functional (disease status) components, but are not limited to this focus. Psychometrically sound, disease specific QOL instruments may prove to be equally sensitive to traditional measures considering the subjective nature of their source. The disabilities resulting from PD are not limited to manifestations of motor function alone. Sleep disturbances, sexual dysfunction, mental status changes are but a few examples of disability which may be related to the disease or from drug therapy and are overlooked in traditional disease focused measurements.

The findings of this study support just such a possibility. In the case of illness impact, 9 of 9 variables had greater percent change improvement than the "gold standard" UPDRS. Illness impact change (improvement) after treatment with tolcapone ranged from 11% improvement to 43% improvement, compared with 2% to 8% improvement in motor UPDRS score. In the case of psychosocial adjustment, improvement ranged from 0% to 33% (see Table 4). Such changes highlight the importance of measurement of quality

of life in evaluative studies of PD. Clearly these findings suggest that patients perceive the impact of their illness in many areas besides motoric function.

The importance of utilizing research findings as a basis for future studies is critical. This study illustrates the importance of evaluative clinical studies which include prior research findings in addition to traditional measures. Maintaining a narrowly focused view on disease symptomatology and indicators, forgoes the rich possibilities of utilizing subject based studies.

One of the most important implications of this study is recognition of the necessity of including quality of life assessment into routine clinical practice. As the shift of health care delivery moves into the out-patient and home setting, nurses will be called upon to assist patients and their families to adapt to the stressors of chronic illness. Though this study has utilized formal research measurement techniques, these same instruments may be used in clinical practice situations as assessment techniques at intake, for follow-up over time, or for determining change or improvement with treatment. Determining change in functional status in chronic illness situations often presents the

clinician with a challenge in trying to quantify change. Use of quality of life measurement will augment assessment with additional and enriched data for determining a plan of care.

Summary

Using repeated measures analysis of variance techniques, this study provided new information on the impact of chronic illness and its' treatment in adjustment to Parkinson's Disease. In addition, it sheds light on the role and relationship of pharmacological treatment in quality of life for patients with Parkinson's Disease.

Health care outcomes will increasingly be measured from the patients point of view. Benefits of treatments and the overall health care system will be judged in terms of the extent to which changes in the patient's functioning or well being meet his/her needs and expectations (Ware, 1992).

The shift in health care delivery, and the focus on the patient rather than disease systems will bring nursing into new partnerships in health care delivery. Focusing on the patient (as a whole entity) is not a new revelation to nursing practice. However, the moment must be seized. Increasing routine nursing assessments to include a broader functional status component will allow for evaluation in

terms of impact on patient functioning and well being in addition to traditionally defined endpoints.

Assisting patients and their families to live successfully, to adapt and cope with the long term effects of chronic illness such as Parkinson's Disease will be a challenge of the future. Nursing has the opportunity to contribute to the delivery of outpatient care, by utilizing research findings such as these to improve the overall quality of patient's lives.

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APPENDIX A

INCLUSION/EXCLUSION CRITERIA OF DOUBLE-BLIND STUDY

APPENDIX A

INCLUSION/EXCLUSION CRITERIA OF DOUBLE-BLIND STUDY

Inclusion Criteria:

1. Onset of PD at age 30 or older.
2. Male or female (surgically sterile or amenorrheic for one year).
3. Patients with predictable ON response to the first daily dose of Sinemet.
4. Patients taking three doses of Sinemet/day, 1:4 ratio, stable for at least one month, with four off periods not including the first off on arising.
5. Patients must be able to complete diaries recording, on, off medication times and demonstrating four or more off periods in 10 hours.
6. Patient must be compliant at least 90% during the placebo baseline period.
7. Patients must sign a written informed consent.

Exclusion Criteria:

1. Patients with atypical Parkinsonian variations.
2. Patients with unpredictable motor fluctuations.
3. Patients with a history of cerebral insult sufficient to cause delayed secondary Parkinsonism.

4. Patients with drug-induced Parkinsonism.
5. Patients with a Hoehn and Yahr stage 4 0r 5 when ON.
6. Patients with resting tremor as the sole manifestation of Parkinson's Disease.
7. Patients with dyskinesias that are severely or completely disabling.
8. Patients with clinically significant hepatic, renal, cardiovascular, endocrinologic, respiratory, neurologic or gastrointestinal disorders, or other current medical problems that may place them at increased risk. This includes people with clinically significant laboratory, vital sign or ECG abnormalities.
9. Patients with psychotic illnesses, chronic psychiatric disorders, drug or alcohol dependence.
10. Patients with intellectual impairment as determined by a score of 25 or less on the Mini-Mental status.
11. Patients treated within the preceding six months with dopamine antagonists.
12. Patients treated within the preceding two months with a MAO inhibitor.

13. Patients treatment within the preceding one month with peripheral dopamine antagonists or any investigational drug.
14. Patients treated within the preceding one month with psychoactive drugs.
15. Patients who are taking indocin, anticoagulants, antidiabetics, phenytoin, pheylbutazone.

APPENDIX B

SICKNESS IMPACT PROFILE

BODY CARE AND MOVEMENT SUBSCALE

APPENDIX B

SICKNESS IMPACT PROFILE

BODY CARE AND MOVEMENT SUBSCALE

Sample Items:

1. I do not maintain balance.
2. I stay lying down most of the time.
3. I do not bathe myself completely, for example, require asistance with bathing.
4. I have trouble getting shoes, socks, or stockings on.
5. I stand only for short periods of time.

APPENDIX C

PSYCHOSOCIAL ADJUSTMENT TO ILLNESS-SELF REPORT

SEXUAL FUNCTIONING SUBSCALE

APPENDIX C

PSYCHOSOCIAL ADJUSTMENT TO ILLNESS- SELF REPORT

SEXUAL FUNCTIONING SUBSCALE

Sample Items:

1. Sometimes when people are ill they report a loss of interest in sexual activities. Have you experienced less sexual interest since your illness?

   a) absolutely no sexual interest since illness

   b) a marked loss of sexual interest

   c) a slight loss of sexual interest

   d) no loss of sexual interest

APPENDIX D

UNIFIED PARKINSON'S DISEASE RATING SCALE

APPENDIX D

UNIFIED PARKINSON'S DISEASE RATING SCALE

Sample Item:

1. Tremor at rest

   0 = absent

   1 = slight and infrequently present

   2 = mild in amplitude and present most of the time

   3 = moderate in amplitude and present most of the time

Face, lips, chin---------

Right arm ---------

Left arm ---------

Right leg ---------

Left leg ---------

APPENDIX E

HOEHN AND YAHR

DISEASE SEVERITY RATING

APPENDIX E

HOEHN AND YAHR

DISEASE SEVERITY RATING

STAGE	0	=	no signs of PD
	1.0	=	unilateral involvement only
	1.5	=	unilateral and axial involvement
	2.0	=	bilateral involvement without impairment of balance
	2.5	=	mild bilateral involvement with recovery on retropulsion
	3.0	=	mild to moderate bilateral involvement some postural instability but physically independent
	4.0	=	Severe disability, still able to walk or stand unassisted
	5.0	=	Wheelchair bound or bedridden unless aided.

APPENDIX F

DEMOGRAPHIC QUESTIONNAIRE

APPENDIX F

DEMOGRAPHIC QUESTIONNAIRE

DATE:_____

PT. CODE:_____

1. Sex: Female____ Male____

2. Date of Birth:_____

3. Marital Status: Single____ Married____

   Divorced/Separated____ Widowed____

4. Year Parkinson's Disease was Diagnosed:_____

5. Education: (Circle Highest Year Completed)

   Elementary thru High School 1 2 3 4 5 6 7 8 9 10 11 12

   College 13 14 15 16 Graduate 17

6. Presently Employed____ Retired____ Seeking Work____

PATIENT: PLEASE LEAVE QUESTIONS BELOW BLANK

Hoehn and Yahr: "ON"_____ "OFF"_____

Total Motor UPDRS: Pre_____ Post_____