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PAIN IN PARKINSON'S DISEASE: CHARACTERISTICS AND RESPONSES IN AMBULATORY CARE PATIENTS

Abstract

Pain is often a disabling symptom in Parkinson's disease (PD), and is currently underassessed, underdiagnosed, and undertreated in this population of primarily older adults. Guided by the Rugh Model of Psychological Components of Pain, an exploration of the characteristics of pain experienced by individuals with PD, and the relationships among the emotional, cognitive, perceptual, and behavioral aspects of pain was undertaken. A convenience sample of 125 patients with PD reporting average daily pain as 2 or greater on the Brief Pain Inventory-Short Form, were recruited for a cross-sectional descriptive survey from two large urban movement disorder centers. Multiple measures were used to assess PD symptoms, depression, attention, beliefs, pain severity, pain interference, quality of pain, and classification of pain symptoms. Multivariable data analyses included descriptive statistics, multiple regression analysis, and correlational techniques. Results demonstrated the strength of the Rugh Model for an examination of pain as a multidimensional experience in PD. Participants reported over two distinct pain symptoms each, with most symptoms classified as musculoskeletal pain. Additionally, most participants described pain as unrelated to idiopathic PD. Correlations with medium to large effect size supported the Rugh Model with significant relationships among pain severity, pain behavior, pain beliefs, depression, sensory quality of pain, and affective quality of pain. Multiple regression analysis demonstrated that 46% of the variance in Pain Interference was explained by pain severity, depression, and pain beliefs. A significant contribution of the study was the use of the International Association for the Study of Pain scheme for coding chronic pain diagnosis modified with M. A. Lee's classification of pain in PD. Intervention trials should integrate assessment for depression in concert with effective strategies for pain management. Clinical research on pain in PD needs to move beyond pain as a sensory symptom and examine pain from a biopsychosocial perspective.

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PAIN IN PARKINSON'S DISEASE:
CHARACTERISTICS AND RESPONSES IN AMBULATORY CARE PATIENTS

Lisette Bunting-Perry

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In

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DEDICATION

To the men and women with Parkinson's disease who have generously given of their time to participate in my study. I endeavor to repay them by heightening the awareness of pain as a nonmotor symptom. I recognize the many sacrifices made by my husband, Jim and our family, as I have dedicated much of our time to the pursuit of scholarly work. To my dear friend and colleague, Gwyn Vernon, thank you for your constant emotional support. Christine thanks for being a wonderful daughter and friend. And lastly, I would like to recognize Jake, the most amazing dog I have ever known.

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ABSTRACT

PAIN IN PARKINSON'S DISEASE:

CHARACTERISTICS AND RESPONSES IN AMBULATORY CARE PATIENTS

Lisette Bunting-Perry

Rosemary Polomano, Dissertation Supervisor

Pain is often a disabling symptom in Parkinson's disease (PD), and is currently underassessed, underdiagnosed, and undertreated in this population of primarily older adults. Guided by the Rugh Model of *Psychological Components of Pain*, an exploration of the characteristics of pain experienced by individuals with PD, and the relationships among the emotional, cognitive, perceptual, and behavioral aspects of pain was undertaken. A convenience sample of 125 patients with PD reporting average daily pain as ≥ 2 on the Brief Pain Inventory-Short Form, were recruited for a cross-sectional descriptive survey from two large urban movement disorder centers. Multiple measures were used to assess PD symptoms, depression, attention, beliefs, pain severity, pain interference, quality of pain, and classification of pain symptoms. Multivariable data analyses included descriptive statistics, multiple regression analysis, and correlational techniques. Results demonstrated the strength of the Rugh Model for an examination of pain as a multidimensional experience in PD. Participants reported over two distinct pain symptoms each, with most symptoms classified as musculoskeletal pain. Additionally, most participants described pain as unrelated to idiopathic PD. Correlations with medium to large effect size supported the Rugh Model with significant relationships among pain severity, pain behavior, pain beliefs, depression, sensory quality of pain, and affective quality of pain. Multiple regression analysis demonstrated that 46% of the variance in Pain Interference was explained by pain severity, depression, and pain beliefs. A significant contribution of the study was the use of the International Association for the Study of Pain scheme for coding chronic pain diagnosis modified with M. A. Lee's classification of pain in PD. Intervention trials should integrate assessment for depression in concert with effective strategies for pain management. Clinical research on pain in PD needs to move beyond pain as a sensory symptom and examine pain from a biopsychosocial perspective.

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CHAPTER 1

Significance of the Problem

Introduction

Parkinson's disease (PD) is a chronic progressive neurologic disease affecting a growing proportion of the aging population. Primarily viewed as a disorder of movement, PD is often accompanied by other symptoms such as pain, depression, and cognitive impairment (Ebrt, Larson, & Aarsland, 2009; Martinez-Martin et al., 2007). Eighty-five percent of adults with PD report pain as the second most troublesome symptom after immobility (M. A. Lee, Prentice, Hildreth, & Walker, 2007); however, pain in patients with PD continues to be underassessed, underdiagnosed, and undertreated (Brefel-Courbon et al., 2009; M. A. Lee, Walker, Hildreth, & Prentice, 2006). Moreover, little is known about the characteristics and time course of pain experienced by individuals with PD, and the relationships of pain to psychological components of the pain experience. The purpose of this study was to describe the source of pain stimuli and classify physiological pain receptor systems in PD, and to investigate interrelationships among the psychological components of pain in adults with PD.

Parkinson's Disease and Pain

With onset typically in the sixth decade of life, PD is the second most common neurodegenerative disorder diagnosed in older adults, after Alzheimer's disease (Strickland & Bertoni, 2004). Approximately 1.5 million Americans are diagnosed with PD and 60,000 new cases are diagnosed each year (Weintraub & Stern, 2005). Tremor, rigidity, bradykinesia, gait, and disturbance in postural control are the classic motor symptoms of PD (Langston, 2006). Pain, however, is increasingly recognized as a disabling symptom in PD and is cited as a major complaint, often prior to confirmation of a PD diagnosis (Quinn, Koller, Lang, & Marsden, 1986; Vaserman-Lehuede & Verin, 1999). Estimates for the prevalence of pain with PD vary considerably, ranging from 40 to 85% (Brefel-Courbon, et al., 2009; Ford, 1998; M. A. Lee, Prentice, et al., 2007). This wide variation in PD pain estimates is related to inconsistent measures of pain, lack of utilization of valid pain measures, and absence of a guiding theoretical framework for pain research. Numerous published reviews provide insight into the difficulties of

assessing and managing pain in PD, which contribute to a limited understanding of the complexity of pain experiences and the impact of pain on physical and psychosocial well-being (Buzas & Max, 2004; Ford & Pfeiffer, 2005; Lanoix, 2009; Negre-Pages, Rezagui, Bouhassira, Grandjean, & Rascol, 2008; Quittenbam & Grahn, 2004; Tinazzi et al., 2006). Furthermore, no universally accepted evidence-based guidelines are available to assist clinicians in the care of individuals with PD who experience painful symptoms (Beiske, Loge, Ronningen, & Svensson, 2009).

Pain is a significant clinical issue in PD, yet a dearth of research is available concerning the problem and sources of painful stimuli. More importantly, information is limited on the multidimensional components of pain in PD and the biopsychosocial effects of this pain. Thus, substantial gaps in knowledge exist about our understanding of a chronic neurodegenerative disease that is disabling and painful. These serious limitations have impeded progress in implementing more effective practices to assess and treat pain from PD.

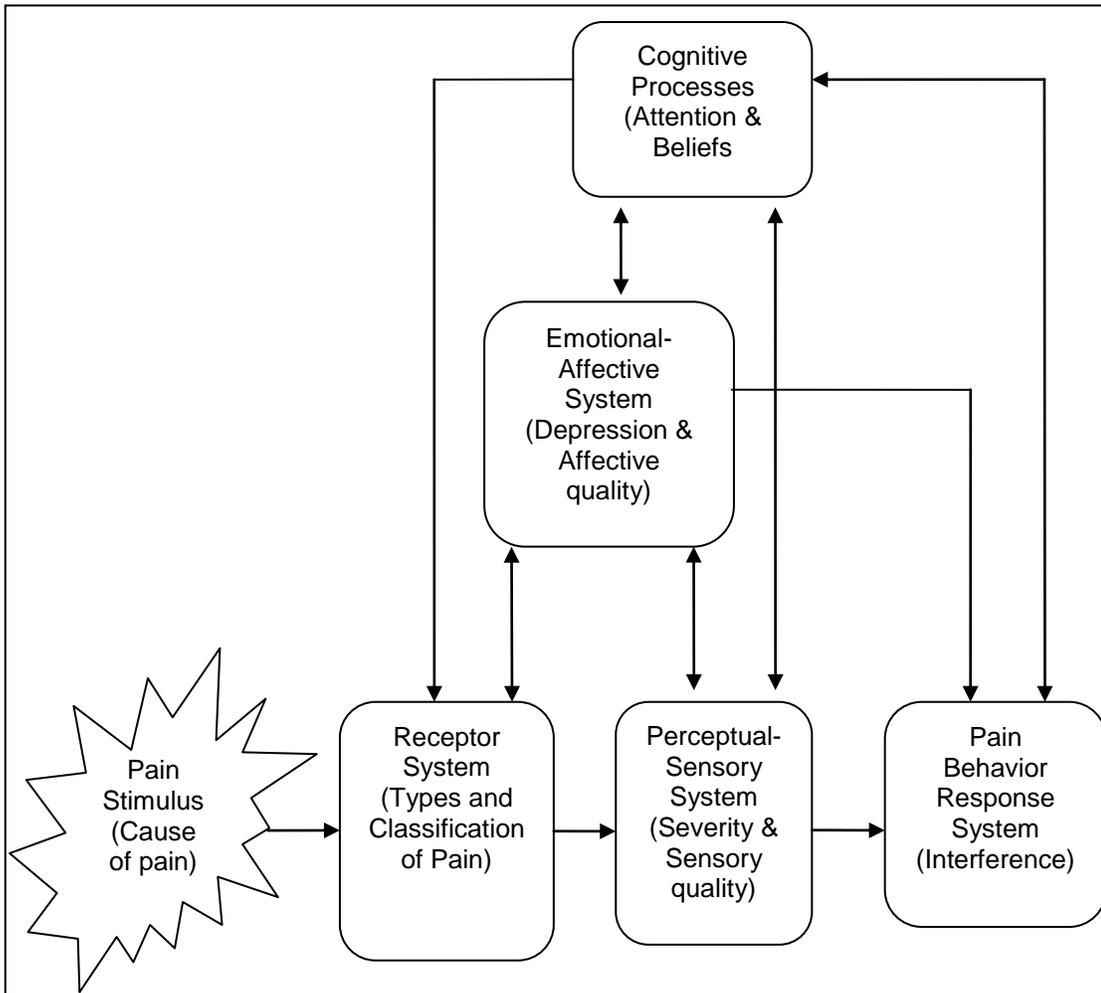
Theoretical Framework

A theoretical framework allows for the structure of scientific inquiry, the framing of research questions, and the explication of relationships among important variables and outcomes influenced by the existence of pain (Gagliese, 2009). Building on Melzack's (1975, 2001) early work, Rugh (1987) constructed a theoretical model to account for the psychological components of pain in dental patients with complex facial pain. Focusing on emotional, cognitive, perceptual, and behavioral aspects of pain, Rugh conceptualized the relationships of the biopsychological perspectives of pain as a multidimensional experience. To date, few theoretical models have been proposed to guide inquiry into the experience of pain in PD. The Rugh Model of the *Psychological Components of Pain*, as modified by the investigator, allows for organizing the multidimensional aspects of pain experienced by adults with PD. Six components from the original model were retained for this investigation to structure the scientific inquiry into pain in PD: 1) *pain stimulus*, 2) *receptor system*, 3) *emotional-affective system*, 4) *cognitive processes*, 5) *perceptual-sensory system*, and 6) *pain behavior response system* (Rugh). The seventh pain component, which extends to the environmental factors affecting pain, is excluded for the

purpose of this study since environmental components of pain were not measured. The Rugh Model was used to organize variables and their relationships.

Figure 1

Rugh (1987) Modified Components of Pain Model. Modified by L. Bunting-Perry with permission (J.D. Rugh, personal communication, February 27, 2008).



Components of Pain and Parkinson's Disease

For many years, pain researchers have focused solely on pain as a sensory experience, neglecting the emotional experience of pain as an unpleasant event. Research on PD and pain has followed a similar path with few studies examining psychological aspects of pain, and purposefully excluding participants with cognitive impairment. Nevertheless, emotion, cognition, perception, and behavior are influenced by pain, and pain in turn affects mood, memory, and activity. There is growing support to view pain as more than just a sensory experience, and interestingly, a multidimensional experience (Gagliese & Melzack, 1997; Melzack & Katz, 2006). Knowledge about the influence of pain on mood, cognition, and adaptation to illness states is limited, however, especially in persons with neurodegenerative disease (Gagliese & Melzack, 2006). For this study, Rugh's (1987) *Psychological Components of Pain* provided a framework to guide conceptual and operational definitions for experiences of pain in PD. Additionally, this model explicated interrelatedness of various concepts under study.

Pain stimulus is conceptually defined as the underlying pathophysiology or possible origin of pain, and is operationalized as injury or disease causing unpleasant sensory symptoms (Pasero, 2004). It is often difficult to identify the etiology or mechanisms for specific pain syndromes associated with PD, as pain symptoms frequently are ill-defined and poorly localized (Ford & Pfeiffer, 2005). A pain stimulus is measured through the identification of PD symptoms, such as muscle tremor, rigidity, dystonia, dyskinesia, or motor fluctuation, which result in pain (Carr, Honey, Sinden, Phillips, & Martzke, 2003; Carroll et al., 2004; Ford, 1998; Hoehn & Elton, 1985; Loher, Burgunder, Weber, Sommerhaider, & Krauss, 2002; Stacy et al., 2005). Other contributory factors to pain stimuli in PD are postural changes imposed by muscular rigidity (Broetz, Eichner, Gasser, Weller, & Steinbach, 2007), and pain associated with traumatic consequences from falls associated with gait and postural control difficulty (Wielinski, Erickson-Davis, Wichmann, Walde-Douglas, & Parashos, 2005). The ability to characterize painful sequelae is also compromised by fluctuations in pain severity because of dopaminergic medications, such as levodopa (Nebe & Ebersbach, 2009; Stacy et al., 2005), and pre-existing

co-morbid conditions causing pain, such as osteoarthritis, postherpetic neuralgia, and peripheral neuropathy (Brefel-Courbon et al., 2009; Sage, 2004; Schmader & Dworkin, 2005).

The *receptor system* is conceptually defined as the detection and transmission of peripheral sensory (pain) information which is modified at spinal levels along sensory pathways of the central nervous system (Woolf, 2004). The *receptor system* is operationally defined as a classification of pain as nociceptive, neuropathic, or a mixed pain syndrome. *Nociceptive* pain is defined as the normal transmission of pain from tissue that is injured or has the potential to be damaged if a pain stimulus is prolonged (McCaffery & Pasero, 1999). Examples of nociceptive pain in PD include pain from persistent tremor, muscular rigidity, and musculoskeletal trauma from falls (M. A. Lee et al., 2006). *Neuropathic* pain is defined as abnormal transmission of pain in the peripheral or central nervous system. Frequent causes of neuropathic pain include diabetic neuropathy, herpes zoster, alcoholic neuropathy, complex regional pain syndrome, and HIV sensory neuropathy (Pasero, 2004). The literature suggests that neuropathic pain in PD is associated with abnormalities in pain modulation related to levodopa therapy and motor fluctuation, such as dystonia and akathisia (Potvin, Grignon, & Marchand, 2009; Tinazzi et al., 2008; Tinazzi et al., 2009).

The *emotional-affective system* is conceptualized as emotional factors that can increase or decrease the nerve impulses from peripheral nociceptors, and thus modify the patient's perception of pain (Rugh, 1987); operationally, it is defined as *depression* and *affective pain experience*. Often overwhelming, pain contributes to depression (Karp, Rudy, & Weiner, 2008; Katz & Melzack, 1999), and has been linked to high rates of suicide in older adults (Tadros & Salib, 2007). Depression, which is prevalent in approximately 40% of individuals diagnosed with PD (Marsh, McDonald, Cummings, & Ravina, 2006), is characterized by a loss of interest in usual activities, decrease in pleasure, or depressed mood (American Psychiatric Association, 2000), and plays an important role in the modulation of pain and pain perception in the elderly (Gagliese & Melzack, 2006). *Affective quality characteristics* are defined as the ability to describe a painful stimulus in terms of tension, fear, and punishment (Katz & Melzack).

Cognitive processes are conceptually defined as attention and beliefs, which influence the perception and reaction to pain (Rugh, 1987). Attention to pain refers to the cognitive ability to focus on pain as a stimulus. Approximately 40% of PD patients develop dementia with a preclinical phase of mild cognitive impairment (MCI) (Caviness et al., 2007); thus, the experience of pain can be significantly affected by changes in cognition. MCI is an intermediate clinical state between normal cognitive aging and mild dementia, and is assessed by brief screening techniques across eight cognitive domains: 1) attention and concentration, 2) executive dysfunction, 3) memory, 4) language, 5) visuoconstructional skills, 6) conceptual thinking, 7) calculations, and 8) orientation (Nasreddine et al., 2005).

Beliefs regarding pain are operationalized as an individual's judgment about painful stimuli as irrelevant, benign, or stressful (Sullivan, Rodgers, & Kirsch, 2001). The theory of *catastrophizing* encompasses pain beliefs (Sullivan, Bishop, & Pivik, 1995), and can serve as a measure for *rumination*, *magnification*, and *helplessness* associated with pain (Sullivan, Lynch, & Clark, 2005; Sullivan, Thorn et al., 2001). Furthermore, "catastrophizing is one of the most important predictors of the pain experience" (Sullivan, Thorn et al., p. 53). To date, no published research on PD and pain has explored beliefs about pain or measured catastrophizing in the context of pain.

The *perceptual-sensory system* is viewed as the recognition of a painful stimulus (Rugh, 1987), and is operationally defined as the ability to recognize the severity and sensory quality of pain (Melzack, 2001). Pain severity is measured by self-report of pain, typically on a zero to 10 scale, indicating *no pain*, to the *worst pain imaginable* (Blozik et al., 2007). Sensory characteristics of pain are measured through word descriptors related to temporal, spatial, pressure, and thermal characteristics (Melzack & Katz, 2006).

Finally, the *pain behavioral response system* relates to the degree to which pain interferes with functioning and disrupts normal activities; it is operationally defined as the patient's self-report of the degree to which pain negatively affects activities, mood, sleep, and enjoyment of life related to actual or anticipated pain (Tan, Jensen, Thornby, & Shanti, 2004). Pain *interference* describes how the experiences of pain can disrupt normal activity, produce decline in function,

and contribute to disability (Gagliese & Melzack, 2006). Little is known empirically about the influence of pain on interference with function in adults with PD.

Purpose of the Study

The purpose of this study was to describe pain stimuli and classify pain *receptor systems* in PD, and to investigate the interrelationships among *cognitive processes* and the *emotional-affective, perceptual-sensory, and pain behavior response systems*. Two specific aims and two research questions frame this inquiry.

Aim no. 1: Characterize signs, symptoms, and manifestations associated with PD that contribute to painful experiences related to clinical PD subtypes (e.g., *tremor-dominant, postural-instability-gait-difficulty, and indeterminate* subtypes), classify *receptor systems* as nociceptive, neuropathic, and mixed pain, and assess pain mechanisms in patients with PD.

Research Question no. 1: What are the relationships and effects of Parkinson's disease (e.g., *tremor-dominant, postural-instability-gait-difficulty, and indeterminate* subtypes), and pain-related pain types (*nociceptive, neuropathic, and mixed*) on participant-reported pain severity?

Aim no. 2: Correlate and compare participant-reported outcomes to identify relationships and differences between and among the *emotional-affective system* (depression and affective quality characteristics), *cognitive processes* (attention and beliefs), *perceptual-sensory system* (pain severity and sensory quality characteristics), and the *pain behavioral response system* (interference) in patients with PD.

Research Question no. 2: What are the relationships among the *emotional-affective system* (depression and affective quality characteristics), *cognitive processes* (attention and beliefs), *perceptual-sensory system* (pain severity and sensory quality characteristics), and *pain behavioral response system* (interference) in patients with Parkinson's disease?

Significance of the Study

A compelling need exists to examine pain in PD beyond the conceptualization of pain as a sensory symptom. Pain, depression, and cognitive impairment are common in PD, contributing to problems in identifying methods of effective assessment and treatment of pain in this unique population. This study was the first to use a theoretical model of pain in PD to investigate the

origins of pain, classify pain symptoms, and examine the relationships among biopsychological components of pain. This approach is useful in elucidating complex phenomena associated with the biopsychological components of pain in PD. Findings provide the basis for future clinical trials on assessment and treatment of pain in PD. It is hoped that this study is the first step in more effective assessment and treatment options for pain in PD, bringing relief to unnecessary suffering in a population primarily composed of older adults.

Table 1 provides a listing of concepts, variables, and measures utilized in the study.

Table 1

Concepts, Variables, and Measures for the Inquiry of Pain in PD

Concepts	Variable	Measure
Pain Stimulus	PD Symptoms	UPDRS
Receptor System	Pain Classification	Revised IASP Taxonomy
Emotional-Affective System	Depression	GDS-SF
	Affective Quality	SF-MPQ Affective
Cognitive Processes	Attention	MoCA
	Beliefs	PCS
Perceptual-Sensory System	Pain Severity	BPI-SF pain severity
	Sensory Quality	SF-MPQ Sensory
Pain Behavior Response	Pain Interference	BPI-SF interference

UPDRS: Unified Parkinson's Disease Rating Scale

Revised IASP Taxonomy: International Association for the Study of Pain (IASP)

GDS-SF: Geriatric Depression Scale Short Form

SF-MPQ: Short Form - McGill Pain Questionnaire

MoCA: Montreal Cognitive Assessment

PCS: The Pain Catastrophizing Scale

BPI-SF: Brief Pain Inventory Short Form

CHAPTER 2

Background and Significance

Introduction

This chapter provides a synthesis and summary of relevant literature on pain and PD, as well as the relationship of pain to emotional, cognitive and behavioral processes in PD. Addressed in this chapter are the gaps in the literature on pain and PD that limit understanding of this significant problem. A brief overview of theoretical models of pain supports Rugh's (1987) Model of the *Psychological Components of Pain* as an appropriate framework for studying the mechanisms of pain associated with PD and the interplay of sensory, perceptual, emotional, cognitive, and behavioral aspects of pain. Classification systems are reviewed for the identification and categorization of painful stimuli in persons with PD. Additionally, psychological influences affecting perception and response to pain are examined and considered within the Rugh framework.

Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey & Bugduk, 1994, p. 210), illustrating the multifaceted nature of pain as a human experience. James Parkinson first reported pain in a patient with PD in his monograph, *An Essay on the Shaking Palsey* (1817):

“A. B. subject to rheumatic affection of the deltoid muscle, had felt the usual inconvenience from it for two to three days: but at night found the pain had extended down the arm, along the inside of the fore-arm, and on the other side of the fingers, in which a continual tingling was felt”. (p. 48)

Parkinson's early narrative presents the protean perspective of pain and elucidates its complexity as a manifestation of the clinical findings associated with PD (Parkinson, 1817). It underscores the importance of the personal nature of pain, and the need to investigate such experiences among older individuals with PD, in order to alleviate unnecessary suffering, disability, and depression.

Review of the Literature

Theoretical Models for the Study of Pain

Pain is a universal, multidimensional experience and considerable strides have been made to advance our understanding of the complexity of pain. Early theorizing about pain in the 19th century was limited to the sensory component (e.g., location and severity), predicated on Descartes' concept of pain published in 1644, one which supported a single pain pathway from the "skin to the brain" (Melzack, 1973, p. 126). This simple theoretical construct of pain formed the basis for the *Specificity Theory* that remained the predominant theoretical framework for the understanding of pain until the introduction of *Summation Theory* accounting for severity of stimuli creating a certain threshold perceived as pain (Melzack, 1973). Neither of these theories explained how pain was processed in the central nervous system (CNS) nor reactions to noxious stimuli. Moreover, early theoretical perspectives failed to account for the complexity of pain as a biopsychosocial experience that is highly influenced by multiple physiological, emotional, and social variables. It was not until 1965 that Melzack and Wall (1965) introduced the *Gate Control Theory*, incorporating physiological specialization, central summation patterning, and modulation of input by psychological factors, which now serves as the basis for current thinking about pain. Melzack and Wall hypothesized that within the spinal cord, gating mechanisms existed to modulate pain, through fast conduction of *A-delta* fibers responsible for closing the gate to decrease pain and slow conduction *C fibers* for opening the gate to increase pain. Thus, the transmission of signals for pain occurred through multiple pathways in the CNS (Melzack & Wall, 1965). Beyond the conduction of pain, Melzack and Wall also proposed the theoretical construct of "perceptual awareness" (p. 976), representing the psychological experience of pain, such as anxiety and attention, which modulates pain in the CNS and affects gating mechanisms.

The *Gate Control Theory* marked a new era for pain research and inspired investigators to build on Melzack and Wall's work in examining pain as a multidimensional experience. In 1987, Rugh published the *Psychological Components of Pain* to fill a void in the theoretical understanding of dental pain. The model, presented in chapter one, explains how attention, emotion, and beliefs influence pain behavior (Rugh). This model explicates relationships among

painful stimuli, perceptual awareness, cognitive processing, and behavioral responses, showing the likely psychological influence of pain on the sensory system and the effects of emotional, cognitive, and perceptual systems on CNS *Gate Control* mechanisms (Rugh).

Current pain research with PD is limited because no unifying theoretical model explains the pain experience in this population. Rugh's (1987) Model of the *Psychological Components of Pain* offers a useful framework for perceptual, cognitive, and behavioral experiences associated with pain in PD. Rugh's Model builds on previous theoretical work in pain and it is particularly relevant to the literature on PD pain, because it includes stimulus and receptor systems, adding to previously unexplored psychological components of the pain experience in PD. The advantage of examining pain in the context of the Rugh Model (Figure 1) is that each component can be observed independently, as well as relationally. The model integrates pain as a sensory symptom along with the understanding of pain as a multidimensional experience.

Stimulus and Etiology of PD Pain

The first component in Rugh's (1987) Psychological Components of Pain is *pain stimuli*. In PD, stimuli are attributed to tremor, rigidity, dystonia, dyskinesia, and related events, such as injury from falls (Carr et al., 2003; Carroll et al., 2004; Defazio et al., 2008; Ford, 1998; Hoehn & Elton, 1985; Lim et al., 2008; Loher et al., 2002; Negre-Pages et al., 2008, Stacy et al., 2005; Broetz et al., 2007; Wielinski et al., 2005). Pain has also been cited as the most common complaint prior to the confirmation of a diagnosis of PD (O'Sullivan et al., 2008), such as shoulder pain (Gilbert, 2004). Despite the linkage of PD symptomatology to pain stimuli, it is difficult to attribute specific causes for pain in PD because of coexisting painful disease states, such as arthritis and orthopedic problems (Brefel-Courbon, et al., 2009; M. A. Lee, Prentice, et al., 2007; M. A. Lee et al., 2006; Negre-Pages et al., 2008; Sage, 2004; Schmader & Dworkin, 2005). In an attempt to bring structure and consistency in pain research, several researchers have developed classifications for pain in PD.

Receptor System and Pain Classification

Pain stimulus leads to *receptor systems* in the Rugh (1987) Model, and provides an opportunity to examine pain through classification schema. Ford (1998) was the first to publish a pain categorization for PD, *Pain by Etiology*. Ford's classification included five types of pain: musculoskeletal, radicular or neuropathic, dystonic, primary or central, and akathetic (defined as physical restlessness) (Ford & Pfeiffer, 2005). Ford's (1998) classification system was supported by a study of 50 patients experiencing motor fluctuations related to the decreased efficacy of Parkinson medications. In the study, 45 individuals with sensory symptoms were classified into seven categories: burning, akathisia, restlessness, neuralgic pain, diffuse pain, tingling, and tightening (Witjas et al., 2002). Elsewhere, in a survey of 101 outpatients with PD, where nearly half reported unpleasant sensory symptoms, pain was described as intermittent, poorly localized, and cramp-like sensations affecting the proximal portion of the limb on the side with the greatest motor deficit (Snider, Fahn, Isgreen, & Cote, 1976). Koller's (1984) study supports Ford's classification with 18 of 50 PD patients reporting sensory symptoms of numbness, pain, burning, aching, tingling, and cold. Other studies confirming Ford's *Pain by Etiology* classification include a study of 95 patients where approximately half described pain as directly related to PD symptoms (Goetz, Wilson, Tanner, & Garron, 1987), a case control study reporting significantly higher frequency of pain in PD patients than age matched controls (Defazio et al., 2008), a study of dyskinetic pain in PD (Lim et al., 2008), and a series of case reports on pain in PD (Ford, Louis, Greene, & Fahn, 1996; Quinn et al., 1986; Silva, Viana, & Quagliato, 2008). Subsequently, a study examining the prevalence and characteristics of pain in PD deployed Ford's classification in a cross sectional study of 176 community dwelling patients with PD (Beiske et al., 2009).

Recognizing limitations of Ford's (1998) classification, M. A. Lee et al. (2006) identified and classified pain in a survey of 123 PD patients in England, mean age 74.3 years, mean duration of disease 6.7 years. Study results first listed the cause of pain as either a neuropathic (5.3%) or nociceptive (94.7%), process and then divided pain according to a schema borrowed from the cancer pain literature. Based on the identification of 285 distinct pain symptoms, mean of 2.3 (± 1.57) per case, a five-item structure was developed for the 285 painful symptoms: 1) pain

related to Idiopathic PD (42.5%), 2) PD treatment related pain (0.3%), 3) pain indirectly related to PD (4.2%), 4) pain unrelated to PD (50.9%), and 5) other or multiple causes of pain (2.1%). The strength of Lee's classification is the conceptualization of PD pain by *receptor systems* based on pathophysiology, pharmacokinetics, co-morbid painful disease states, and the classic theories of pain.

Unfortunately, neither Ford (1998) nor M. A. Lee et al. (2006) support their classifications solidly on the science of pain as documented in the literature. As early as 1987, members of the International Association for the Study of Pain (IASP) published a sophisticated categorization of pain as a method to organize mechanisms and manifestations of pain within a five axis system. The IASP system categorizes pain through the following taxonomy: Axis I - anatomical region or site affected by pain, Axis II - system producing pain, Axis III - temporal characteristics of pain, Axis IV – patient's report of pain severity, and Axis V – pain etiology (Merskey & Bogduk, 1994; Turk & Rudy, 1987). Such a classification of pain standardizes clinical and research findings, ultimately providing consistent measures from comparisons of outcomes in clinical trials (Derasari, 2003). The IASP method is not designed as an assessment of pain, but it is a multidimensional guide incorporating sensory symptoms of pain. Nor does it include a psychological assessment of pain (Turk & Rudy). Thus, a study of pain in PD can be strengthened by integration of Ford's (1998) and M. A. Lee's (2006) work with the contemporary IASP classification of pain (Merskey & Bogduk) in order to be consistent with current science.

Psychological Components of Pain

The experience of pain as a sensory stimulus is influenced by emotion, cognition, perception, and behavior and is further affected by the relationships among these components. Few studies of PD have investigated psychological influences of pain or the complex relationships among depression, pain affective quality, attention, pain beliefs, pain severity, pain sensory quality, or interference from pain. The inclusion of psychological aspects of pain in the Rugh (1987) Model provides a new perspective for the inquiry of pain in PD. In the following section, general pain literature focusing on pain in older adults is reviewed to demonstrate the influence and role of emotion and behavior on pain with PD.

Emotional-Affective System

Emotional factors, such as depression or the affective quality of pain symptoms can increase or decrease nerve impulses from peripheral nociceptors, and modify the perception of pain. Rugh's (1987) Model includes specific components that allow a more thorough examination of affect and mood in relationship to pain.

Depression. As part of the *emotional-affective system* of pain, depression is recognized as a significant factor in the experience of pain, especially in older adults (Geerlings, Twisk, Beekman, Deeg, & van Tilburg, 2002; Roh et al., 2009). Several studies cite higher levels of depression in PD patients experiencing pain (Goetz et al., 1987; Urakami et al., 1990), whereas others report an association between severity of depression and increased pain in PD (Ebrt et al., 2009; M. A. Lee et al., 2006; Starkstein, Preziosi, & Robinson, 1991). The association between depression and pain is complex with most researchers supporting a bidirectional relationship (Karp et al., 2005). Two studies examining motor complications in PD, however, found no meaningful relationship between depression and pain (Letro, Quagliato, & Viana, 2009; Tinazzi et al., 2006).

Affective Quality of Pain. In pain research, the affective quality of pain is determined by ability to describe pain in terms of tension, fear, and punishment. A standard measure for quantifying this dimension is the Affective subscale of the Short-Form McGill Pain Questionnaire (SF-MPQ). Studies on PD and pain have utilized the MPQ in a treatment study for dyskinesia (Carroll et al., 2004) and a pain threshold investigation (Massetani, Lucchetti, Vignocci, Siciliano, & Rossi, 1989). The MPQ (Melzack, 1983) was cited in two PD pain surveys (Goetz, Tanner, Levy, Wilson, & Garron, 1986; Letro et al., 2009), a treatment study of botulinum toxin for dystonic pain (Pacchetti et al., 1995), a correlational study of sleep, pain, and depression in PD (Starkstein et al., 1991), and a study examining PD patients in the *on* and *off* levodopa state (Nebe & Ebersbach, 2009). Nebe and Ebersbach reported PD patients associated pain symptoms with affective words of fear (87%) and punishment (87%). Pacchetti et al. were the only investigators to identify "exhausting" as a tension category for affective descriptors (Melzack & Katz, 2006) of dystonic pain in a sample of 30 adults with PD. This finding was also supported

in a study comparing older, $n = 139$, mean age $70.1 (\pm 7.5)$ and younger, $n = 139$, mean age $42.9 (\pm 9.4)$, patients with low back pain and arthritis, using the following quality words to describe pain: punishing-viscous (30%), fearful-terrifying (20%), sickening-suffocating (18%), and tiring-exhausting (70%) (Gagliese & Melzack, 2003). No significant differences were noted in the frequencies of word selections between the older and younger age groups in describing pain (Gagliese & Melzack).

Cognitive Processes

Pain is influenced by our ability to pay attention to stimuli and by our beliefs in our ability to manage or control pain. The ability to process pain cognitively influences our perception and reaction to it.

Attention. The capacity to pay attention to pain perception is driven by beliefs regarding the perceived threat and the need to initiate adaptive behavior (Van Damme, Crombez, & Eccleston, 2004a, 2004b). The Rugh (1987) Model provides a framework for these relationships among *cognitive processes*, *perceptual-sensory systems*, and *pain behavior*. The relationships among these variables are emerging as an important construct in the pain literature and are considered a priority for research on the physical and psychological components of pain (G. K. Lee, Chan, & Berven, 2007; Leeuw et al., 2007).

The cognitive process of registration and attention to pain is a significant attribute in pain science, particularly in clinical research with older adults (Scherder, Oosterman et al., 2005). Cognitive impairment has been an exclusion criterion in PD pain research, typically set by a Mini Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975) score of < 24 out of 30 in studies of levodopa modulated pain (Brefel-Courbon et al., 2005; Defazio et al., 2008; Gerdelat-Mas et al., 2007a; Mylius et al., 2009; Negre-Pages et al., 2008), pain perception (Djaldetti et al., 2004), a survey of motor complications (Tinazzi et al., 2006), and a correlational study of sleep, pain, and depression (Starkstein et al., 1991). Most published research on PD and pain does not include an assessment of cognitive status, and the few published studies with information on cognition show minimal differences in MMSE scores in an attempt to control for group differences in research design (Urakami et al., 1990). Several studies provide reports of MMSE scores with

no detail on variations in levels of cognition or the impact on other variables such as pain, physical mobility, dystonia, or PD motor symptoms (Karlsen, Tandberg, Arslan, & Larsen, 2000; Witjas et al., 2002). In a study comparing PD patients with pain (n = 152) to PD patients without pain (n = 75), those with painful symptoms have significantly lower MMSE exam scores ($p < .001$) (Ebrt et al., 2009). Clearly more research is needed to characterize cognitive impairment, and the degree to which attention deficits affect the perceptual aspects of pain in PD.

The underreporting of pain by older adults with cognitive decline is well established in the pain literature; however, the association of attention deficits or their severity to underreporting is debated by leading scholars (Schuler, Njoo, Hestermann, Oster, & Hauer, 2004). The predominant theory is that older adults with cognitive impairment are less able to pay attention to and verbalize pain symptoms, leading to inadequate assessment and undertreatment of pain (Hadjistavropoulos et al., 2007; Herr et al., 2006; Herr, Spratt, Mobily, & Richardson, 2004). Others suggest that pathophysiological brain changes affect the registration of pain in the medial pain system (thalamic intralaminar nuclei) (Scherder, Sergeant, & Swaab, 2003; Scherder, Wolters, Polman, Sergeant, & Swaab, 2005). This is supported in studies of pain in older adults with Alzheimer's disease, which demonstrate lower pain severity compared to normal controls (Scherder, Oosterman et al., 2005). Likewise, in the basal ganglia, at the center of research on PD motor symptoms, neurodegeneration has been cited as contributing to abnormal pain, from hypofunctioning of the dopaminergic system (Chudler & Dong, 1995; Hagelberg et al., 2004; Lim et al., 2008; Mylius et al., 2009; Nebe & Ebersbach, 2009; Potvin et al., 2009; Schestatsky et al., 2007; Tinazzi et al., 2008; Tinazzi et al., 2009; Wood, 2008). Investigations of pain in PD offer a unique opportunity to generate insights into how pain is perceived and communicated in neurodegenerative brain disease processes, but where language skills are preserved despite declines in cognitive function (Caviness et al., 2007). The ability of patients with PD to pay attention to and express verbally their pain experiences allows for a more distinct characterization of pain compared to those with pronounced cognitive deficits, as with Alzheimer's disease.

Mild cognitive impairment is evident in approximately 20% of PD patients (Caviness et al., 2007), and is defined as a preclinical state preceding the onset of dementia (Nasreddine et

al., 2005) usually seen in the later stages of PD. It is generally characterized by deficits in a single domain of cognition with frontal/executive deficits being the most common (Caviness et al.). Mild cognitive impairment in PD can be measured by the Montreal Cognitive Assessment, which is sensitive to the subtle changes in early cognitive decline (Zadikoff et al., 2008). To date, there is no compelling evidence to support that mild cognitive impairment interferes with accurate or reliable self-report of pain (Fisher, Burgio, Thorn, & Hardin, 2006; Simmons, Ferrell, & Schnelle, 2002). Patients with PD have six times the likelihood of developing a full dementia syndrome as compared to normal controls, with prevalence estimates of 31% (Janvin, Larsen, Aarsland, & Hugdahl, 2006). Deficits in short-term memory, along with frontal/executive dysfunction, are the principle signs observed in PD patients experiencing mild cognitive impairment (Caviness et al.).

In a study of 56 older adults in a pain management clinic, mean age 76.1 (± 8.6), a significant relationship existed between pain severity scores (SF-MPQ) and executive dysfunction (number-letter switching) (Karp et al., 2006). Another study of 149 chronic pain inpatients, mean age 59.2 (± 14.96) years, frequent memory complaints were significantly related to levels of depression ($r = .60, p < .001$) and pain catastrophizing ($r = .47, p < .001$) (Munoz & Esteve, 2005). Likewise McCracken and Iverson (2001) found significant relationships between increased cognitive complaints and higher pain severity ($r = .24, p < .001$) and higher depression ($r = .54, p < .001$) in a study of 275 consecutive patients referred to a large university pain center.

Beliefs. Theoretical models incorporating psychosocial components of pain often include variables on pain beliefs. An emerging construct is *catastrophizing*, defined as “a coping strategy, a belief, or an appraisal process” (Sullivan, Thorn et al., 2001, p. 57) that is “an exaggerated negative mental set brought to bear during actual or anticipated painful experience” (p. 53). Early conceptual work on *catastrophizing* emerged from dental literature describing patients with catastrophic thoughts as more likely to experience distress during dental procedures (Chaves & Brown, 1987). Catastrophizers are described as “exaggerating the threat value of pain sensation” (Sullivan, Thorn et al., p. 53).

The first psychometric measure of *catastrophizing* examined helplessness and pessimism in a subscale of the Coping Strategies Questionnaire (CSQ) (Rosenstiel & Keefe,

1983). Subsequently, numerous studies using the CSQ demonstrated a positive relationship between high levels of catastrophic thinking and higher levels of emotional and physical distress in patients with musculoskeletal pain (G. K. Lee et al., 2007), general chronic pain (Edwards, Smith, Kudel, & Haythornthwaite, 2006; Jensen, Turner, & Romano, 2007), and spinal cord injury (Ullrich, Jenson, Loeser, & Cardenas, 2007). Expanding on the construct of *catastrophizing*, Sullivan et al. (1995) developed the Pain Catastrophizing Scale (PCS) to incorporate current pain literature in a comprehensive measure. A factor analysis with oblique rotation was performed on correlations between the PCS and four established measures: 1) Fear of Pain Questionnaire, 2) State-Trait Anxiety Inventory – Trait Form, 3) Beck Depression Inventory, and 4) the Positive Affective-Negative Affect Scale in a study of 28 patients at a rehabilitation center, mean age 40 (± 8.7) (Sullivan et al., 1995). The factor analysis supports three domains of pain catastrophizing: *ruminatation* - "I can't stop thinking about how much it hurts"; *magnification* - "I worry that something serious may happen"; and *helplessness* - "It's awful and I feel it overwhelms me" (Sullivan, 2004, p. 4). Further oblique factor analysis of the PCS was conducted in adult samples using correlations between the three PCS subscales and the Positive Affective-Negative Affect Scale (PANAS) (Osman et al., 2000). In the first sample of 215 individuals in the community, a survey was randomly distributed to homes by zip code, n = 85 males, mean age 35.9 (± 10.8), range 20-59 years; females n = 130, mean age 34.6 (± 12.2), range 20-65 years; the second sample was obtained from an outpatient pain clinic, n = 26 males, mean age 31.2 (± 8.7), range 19-52 and n = 34 females, mean age 33 (± 10.7), range 19-53 years (Osman et al.). Results supported PCS correlation with measures of pain severity ($r = .51, p < .001$) and less so with the PANAS Negative Affect subscale ($r = .31, p < .001$) (Osman et al.).

The PCS has been used extensively in pain research and generates continuous level data (Sullivan, Thorn et al., 2001) about catastrophizing, pain severity (Denison, Asenlof, Sandborgh, & Lindberg, 2007; Sullivan, Martel, Tripp, Savard, & Crombez, 2006; Sullivan, Stanish, Waite, Sullivan, & Tripp, 1998), depression (Munoz & Esteve, 2005; Sullivan, Rodgers et al., 2001), and interference with activities (Denison et al., 2007; Osborne, Jensen, Ehde, Hanley, & Kraft, 2007; Sullivan et al., 2005; Sullivan et al., 1998). Greater catastrophizing scores have

been consistently associated with higher pain severity, increased depression, and diminished psychological and physical function. Although the concept of catastrophizing has not been studied specifically in older adults, the construct has been evaluated in investigations of musculoskeletal pain. In particular, a study using a large community-based sample (N = 1,164) found no significant correlation between catastrophizing and age ($r = .02$); however, a statistically significant relationship was noted between catastrophizing and pain severity ($r = .31, p < .01$) (Severeijns, Vlaeyen, van den Hout, & Picavet, 2004). Similarly, in an investigation of 80 adults with neuropathic pain (mean age 53, range 24 -84 years) no significant association was found between age and catastrophizing, suggesting that the construct is relatively unaffected by age (Sullivan et al., 2005). As part of a randomized, crossover clinical trial to evaluate the effects of opioids and tricyclic antidepressants for the treatment of post-herpetic neuralgia, N = 68, mean age 71 (± 12), range 32 - 90; pain, interference, coping, and catastrophizing and their relationships to adaptation to illness were examined (Haythornthwaite, Clark, Pappagallo, & Raja, 2003). The regression model was designed to predict pain ratings at week eight of the trial and included baseline pain ratings (zero to 10), perceived interference from pain (Interference subscale of the Multidimensional Pain Inventory), physical activity (Activity subscale of the Multidimensional Pain Inventory), and depression (Beck Depression Inventory), which accounted for 25% of the variance in pain ratings ($p < .001$) (Haythornthwaite et al.). Further analysis, adding coping strategies to the regression model as a dependent variable, indicated catastrophizing at baseline accounted for an additional 6% of the variance in pain ratings ($p < .05$) (Haythornthwaite et al.).

From a conceptual perspective, the construct of catastrophizing has been criticized because of a potential overlap with measures of depression (Severeijns, van den Hout, Vlaeyen, & Picavet, 2002). Recent studies, however, indicate that catastrophizing is a separate and distinct construct from depression and a dynamic intervening variable for pain (Haythornthwaite et al., 2003; G. K. Lee et al., 2007; Sullivan, Rodgers et al., 2001; Sullivan, Thorn et al., 2001).

Perceptual-Sensory System

The perception of pain is communicated by self-report of severity and can be measured in numerous ways to capture what Melzack and Wall (1996) refer to as the “language of pain” (p. 36). The quantification of pain severity in research can be a simple rating of pain as mild, moderate, or severe, or something more complex, such as verbal descriptors of mild, discomforting, distressing, horrible, or excruciating (Melzack & Wall).

Pain Severity. A common method of measuring pain severity is the visual analog scale (VAS), where participants make a mark on a ten-centimeter vertical or horizontal line to indicate the level of pain from *no pain* to *worst pain imaginable* (Melzack & Wall, 1996, p. 37). This technique has been used in numerous studies on PD and pain. Examining back pain in PD, Broetz et al. (2007) reported significantly higher pain severity VAS scores ($p < .001$) in PD patients, mean VAS 4.3/10, $n = 101$, median age 68, range 40-89) compared to age sex matched controls (mean VAS 1.3/10, $n = 132$, median age 65, range 40-88). In a similar study, Echeperare et al. (2006) compared 104 PD patients, mean age 66 (± 9) years, with 100 controls, mean age 65 (± 10) years, in a cross-sectional survey of back pain. Prevalence of back pain was 59.6% in the PD group compared to 23% in the control group ($p < .001$). Average severity of back pain was rated on a 100 mm line and found to be significantly higher ($p < .001$) in the PD group, mean VAS 54 (± 23) than in controls, mean VAS 41 (± 19) (Etchepare et al., 2006). Likewise, Defazio et al. (2008) reported a mean pain severity of six, for dystonic pain, among PD patients in a case controlled study comparing pain in PD participants, sample size of 402, age 67.4 (± 9.1) to sex/age matched controls, sample size of 317, age 65.5 (± 10.4) years. Dystonic pain was absent in the control group (Defazio et al.). In contrast, Quittenbaum and Grahn (2004) found no significant differences in VAS pain severity scores in a mailed survey to 57 PD patients, mean age 70.1 (± 8.8), and 95 controls, mean age 70.1 (± 8.3), where participants recalled pain severity over the past month.

Using Ford's (1998) classification of pain in PD, Tinazzi et al. (2006) measured the VAS scores in 117 patients, mean age 69.4 (± 8.1), of which 47 (40%) reported pain. Pain was rated

more severe for patients with dystonic pain, $n = 19$, mean VAS 7.1 (± 1.4), as compared to patients with musculoskeletal pain, $n = 10$, mean VAS 6.5 (± 1.5) or radicular neuritic pain, $n = 4$, mean VAS 5.3 (± 3.0) (Tinazzi et al.). M. A. Lee et al. (2006) are the only investigators to report pain severity using the Brief Pain Inventory (BPI) and a 100 mm VAS measure of pain, mean VAS 38.9 (± 25.4), range 0-95, in a cross-sectional interview with 123 PD patients, mean age 74.3, range 51-89 years. Pain was rated as *its worst* and *on average* in the past 24 hours using the BPI pain severity scale (zero to 10) and pain was rated for the past week on a VAS scale. BPI pain ratings were categorized as no pain = 0, mild pain 1 – 4, moderate pain 5 - 6, and severe ≥ 7 , and results were analyzed by multiple regression (M. A. Lee et al.). Average pain (BPI) and VAS scores were identified as outcome variables in the regression model, using age, stage of disease, disease duration, MMSE, and number of symptoms (measured by the Palliative Care Assessment scale) as possible predictors. Pain severity (VAS) was predicted by number of symptoms (measured by the Palliative Care Assessment scale) (beta coefficient = .25, $p < .02$). Age, stage of disease, disease duration, or MMSE scores did not explain any significant portion of the variance in pain severity (M. A. Lee et al.).

The relationship between pain and depression is documented in studies of pain severity with PD. Starkstein et al. (1991) reported that pain was more severe in PD patients with major depression, $n = 13$, mean age 67 (± 8.2), compared to those with mild depression, $n = 9$, mean age 65.6 (± 9.6) or no depression, $n = 57$, mean age 68.3 (± 8.7), as measured by the Modified McGill Pain Questionnaire, $p < .05$ (Melzack, 1983). In contrast, Goetz et al. (1997) did not find a relationship between patient reports of pain severity, measured by the McGill Pain Questionnaire, and depression ($r = .16$, $p > .20$), measured by the Beck Depression Inventory; however, patients with pain were more depressed than patients without pain. Likewise, Defazio et al. (2008) found PD patients with painful symptoms had higher levels of depression ($p = .001$), measured by the Beck Depression Inventory, and higher number of painful co-morbid disease states ($p = .02$) as compared to age/sex matched controls.

Sensory Quality: Measuring pain on the single dimension of *severity* limits the understanding of pain *quality* as a multidimensional experience. Words describing the *sensory*

quality of pain are useful in communicating pain complaints from the perspective of temporal, spatial, pressure, and thermal properties. In several studies of PD pain, patients assigned word descriptors such as cramping, aching, or burning (Bulpitt et al., 1985; Defazio et al., 2008; Hoehn & Elton, 1985; Koller, 1984; Snider et al., 1976; Stacy et al., 2005). The most well known method to measure the *sensory quality* of pain is the Sensory subscale of the SF-MPQ. Melzack's research has supported the assumption that sensory words used to describe pain can predict medical diagnosis (Melzack & Wall, 1996).

Using a revised version of the McGill Pain Questionnaire, Goetz et al. (1986) conducted a survey of 95 Parkinson patients (mean age of 66.3 years) and described pain in PD as burning, numbness, and tingling, with pain severity scores peaking when Parkinson medications were wearing *off*. Interestingly, Goetz et al. was the first to describe younger PD patients (mean age 62 years) reporting more pain than older patients (mean 68 years, $p < .005$). Pacchetti et al. (1995) also used the McGill Pain Questionnaire to describe sensory words for dystonic pain in PD as wrapping, cramp-like, and stinging. These narrative words describe how painful sensations in PD may interfere with daily activity.

Pain Behavior Response

Most behavioral responses to pain stimuli are normal protective mechanisms (Montes-Sandoval, 1999), but unfortunately, pain behaviors may become problematic when activities are restricted, contributing to decreased mobility, fear of pain, depression, and dependence on others (Breen, 2002; Leeuw et al., 2007). The study of behavioral responses to painful stimuli in older adults is an emerging area of research, and may assist in identifying interventions to manage chronic pain in this population (Parmelee, 2005).

Interference Pain Behavior. The concept of pain interference is not well defined, and is often associated with function or disability (Thomas E. Rudy & Lieber, 2005). For the purpose of this study, pain interference is conceptualized by the structure of the BPI-SF Pain Interference subscale which measures the degree to which pain interferes with activity, mood, ambulation, work, relationships, sleep, and enjoyment of life (V. S. Williams, Smith, & Fehnel, 2006). This broad concept of pain interference, as measured by the BPI-SF, converges with literature on pain

related to quality of life (Fortner et al., 2003), sleep (V. S. Williams et al., 2006), depression (G. K. Lee et al., 2007), disability (Leeuw et al., 2007), and function (Karloly & Ruehlman, 2007).

Little empirical evidence exists for the association between pain and behaviors in PD, specifically, how pain interferes with daily life. M. A. Lee et al. (2006) used the Wisconsin Brief Pain Questionnaire in a survey of pain in PD, but provided no details on the results from the Pain Interference subscale noting that “85% of patients reported pain as a problem over the last week and 50% said it was moderate or dominating their day” (p. 464). Communication with Lee helped clarify his perspective on how the BPI-SF Pain Interference subscale could be viewed as an acceptable measure of pain interference - “Patients with PD are able to distinguish whether it is pain or other issues (e.g. bradykinesia), which interfere with function” (M. A. Lee, personal communication, June 26, 2008). Negre-Pages et al. (2008) found significantly higher levels of BPI-SF Pain Interference subscale scores in patients with pain related to PD (n =167) as compared to PD patients with pain from other causes (n =111). Results were significant for four items of the BPI-SF Pain Interference subscale 1) interference in general activity (p = .007), 2) mood (p = .004), 3) relationships with others (p = .02) and 4) interference with enjoyment of life (p < .001).

Goetz et al. (1986) reported that pain in PD was disabling, interfering with daily activities, and was positively correlated to motor fluctuations in motor symptoms and measures of disability. Likewise, Broetz et al. (2007) described back pain as a common cause of impairment in activities of daily living in PD patients as compared to age-matched controls with stroke or brain tumors, p < .001. Pain interference was also explored in several studies investigating pain in rehabilitation literature. One study examined VAS pain severity scores predicting interference with daily activities in a study of rehabilitation patients (N = 171) with musculoskeletal pain, mean age 42.5 (± 9.9) (G. K. Lee, Chan & Berven, 2007). Ullrich et al. (2007) described psychological distress and pain severity as independent predictors of pain interference, as measured by the BPI, in a mailed survey of patients with spinal cord injury (N = 237), mean age for females 45.3 (± 13.7), mean age for males 47.51 (± 12.9). Likewise, all subscale pain interference items on the BPI were

significantly correlated with average pain severity in a study of patients with cerebral palsy, $N = 50$, mean age 39.7 (± 13.0) (Tyler, Jensen, Engel, & Schwartz, 2002).

Finally, it is worth reviewing three studies that exemplify the inquiry of psychological factors of pain and function. Denison et al. (2007) identified three clusters in profiling physical therapy patients with musculoskeletal pain in two samples. Sample one had a sample size of 215, mean age 45 (± 13), range 19-65 and sample two had a sample size of 161, mean age 47 (± 11), range 20-65. The first cluster (43% of the sample) was described as having low levels of pain severity, low disability, and high levels of self-efficacy with low levels of fear of reinjury and low catastrophizing. The second cluster (35% of the sample) demonstrated high pain severity and disability scores with low self-efficacy, low fear of reinjury, and low catastrophizing scores. The last cluster (22% of the sample) demonstrated high pain severity and disability with low self-efficacy, high fear of reinjury and high catastrophizing. Through this study, it was possible to construct a model for depicting relationships among psychological components of pain. Sullivan et al. (2005) also developed a regression model examining neuropathic pain in 80 patients (mean age 52.5 years, range 24-84 years), including measures of spontaneous pain (SF-MPQ), evoked pain (VAS) by tactile allodynia and pinprick hyperalgesia, pain catastrophizing (PCS), and functional disability (Pain Disability Index). This regression model suggested pain catastrophizing predicted functional disability (Sullivan et al.). The last study examined a model of psychological and environmental factors of pain in patients with multiple sclerosis (MS), $N = 125$, mean age 50.79 (± 10.8) years (Osborne et al., 2007). The regression model included MS disease related characteristics, pain severity (average pain from zero to 10), pain interference (BPI subscale), psychological function (Mental Health scale from the SF-36), pain coping (Chronic Pain Coping Inventory), pain cognitions and beliefs (Catastrophizing subscale of the Coping Strategies Questionnaire), and social support (Multidimensional Scale of Perceived Social Support). In the regression model predicting pain interference scores (BPI-SF Pain Interference subscale) only MS disease severity was a significant independent predictor of pain interference ($B = 0.31$, $p < .001$). When psychosocial variables (social support, catastrophizing, pain beliefs, and pain coping) were added to the regression model, they accounted for 22% of the variance in BPI

interference scores ($R^2 = .22$, $F = 10.37$, $p < .001$). Univariate analysis demonstrated catastrophizing was related to pain severity ($r = .31$, $p < .003$), interference ($r = .44$, $p < .003$), and psychological functioning ($r = -.53$, $p < .003$) (Osborne et al.). These three studies show the complex relationships among components of pain, related symptoms, and outcomes with PD.

Sex, Race, and Age

Little attention has been paid to sex, race, or age in regard to pain in patients with PD; however, the sample available for this study limited examination of these important variables. A large descriptive study, examining distressing Parkinson symptoms, identified neck and back pain as the most troublesome symptoms for females ($n = 356$) compared to tremor, rigidity, and fatigue identified by males ($n = 590$) (Scott, Borgman, Engler, Johnels, & Aquilonius, 2000). Defazio et al. (2008) found no sex differences in pain among PD patients ($p = .23$) in a large case controlled study of pain and PD. Beiske et al. (2009), however, found sex to be a predictor of pain in females with PD ($p = .006$). Overall there is a dearth of information on racial differences in PD research, despite a significant increase in the Hispanics population (Van Den Eeden et al., 2003). The influence of age on PD is rarely addressed, as clinical research is typically conducted on younger participants with fewer co-morbid diseases.

Examining the influence of age on pain in patients with PD is an important research priority; unfortunately, published PD pain investigations do not present sufficient variability in age and data are not available to address this issue. Prior research on variation of pain in the general pain literature examined three age groups, young ($n = 143$, age 18 – 39 years), middle age ($n = 195$, age 40 – 59 years) and older ($n = 116$, age 60 – 81 years). Findings suggest chronic pain is more prevalent in older adults (31%) compared to middle-aged adults (25%). The older group had significantly greater co-morbid disease, but rated quality of life higher than the middle-age chronic pain group (Rustoen et al., 2005). Future research may provide an opportunity to examine differences in sex, race, and age in the experience of pain in patients with PD by including women and younger adults from settings with a diverse composition.

Summary

Pain with PD is poorly understood, despite the fact that this is a common and complex problem. A review and synthesis of literature on PD and pain, as well as other related literature, supports the interrelatedness of components of the pain experience defined by Rugh's (1987) Model of the *Psychological Components of Pain*. Moreover, there is emerging research in the components of pain identified by Rugh to justify further exploration into the causes of pain in patients with PD, refinement of classifications for pain manifestations and symptoms associated with the disease and its treatment, and examination of relationships among psychological components of pain such as emotions, beliefs, and catastrophizing about pain. A better understanding of pain in patients with PD will explicate the various components of that pain and allow for addressing pain as a clinical priority, thus assisting clinicians in the use of a common nomenclature for pain and targeting more effective treatments. Likewise, the relationships among the *emotional-affective system* (depression and affective quality characteristics), *cognitive processes* (attention and beliefs), *perceptual-sensory system* (pain severity and sensory quality characteristics), and *pain behavioral response system* (interference) deserve attention if intervention-based strategies to improve function and quality of life for older people with PD are to be developed, tested, and used routinely in clinical practice.

CHAPTER 3

Research Methodology

Research Design and Methods

A cross-sectional descriptive design was used to identify and describe patterns and relationships among pain constructs in adults with PD. In order to elucidate the pain experience a variety of questionnaires and instruments were administered to a convenience sample of individuals diagnosed with idiopathic PD at two large movement disorder centers. The specific aims of the study were:

Aim no. 1: Characterize signs, symptoms, and manifestations associated with PD that contribute to painful experiences related to clinical PD subtypes (e.g., *tremor-dominant*, *postural-instability-gait-difficulty*, and *indeterminate* subtypes), classify *receptor systems* as nociceptive, neuropathic, and mixed pain, and assess pain mechanisms in patients with PD.

Aim no. 2: Correlate and compare participant-reported outcomes to identify relationships and differences between and among the *emotional-affective system* (depression and affective quality characteristics), *cognitive processes* (attention and beliefs), *perceptual-sensory system* (pain severity and sensory quality characteristics), and the *pain behavioral response system* (interference) in patients with PD.

Sample

A convenience sample of 125 individuals with idiopathic PD, who rated *average* pain as two or greater on the Brief Pain Inventory Short Form (BPI-SF), were recruited from the Philadelphia Veterans Affairs (VA) Parkinson's Disease Research Education and Clinical Center (PADRECC) (n = 29), and the University of Pennsylvania Parkinson's Disease and Movement Disorders Center (PD & MDC), located at Pennsylvania Hospital (n = 96). The sample consisted of English speaking individuals with a diagnosis of idiopathic PD. The diagnosis of PD was confirmed by a movement disorder specialist and documented in the medical record. Eligible participants were able to identify painful sensory symptoms on the pain severity question of the BPI, reporting pain as a *two* or greater for *average pain*. Study participants were capable of reading and understanding the consent, independently answered questions regarding the study,

signed the consent form, and participated in an interview. Participants agreed to take part in a study procedure lasting up to two hours.

Settings

The PVAMC PADRECC was founded in 2001 as one of the original six PADRECCs in the VA Health Care System to improve health care services to veterans with PD and related disorders. The Philadelphia PADRECC provides care for veterans from the Northeastern corridor of the United States and has served over 1800 patients since its establishment. The PADRECC is recognized for an innovative clinical care model, providing patients with comprehensive care at each visit. The center is staffed by an interdisciplinary team of: three movement disorders specialists, a geriatric psychiatrist, physiatrist, four clinical nurse specialists, social worker, speech pathologist, pharmacist, and neuropsychologist. A review of 824 records, from the PADRECC administrative database, yielded a sample of older (mean age 75 years), Caucasian (76%) males (98%). Fifty-one percent had a diagnosis of PD (J. Lumford, personal communication, June 19, 2008). The available PADRECC sample is not generalizable to women, minorities, or younger patients with PD. Current PADRECC cases represent less than 25% minorities, reflective of national trends of patients followed in movement disorder centers in the United States. In fiscal year 2007, 160 new consults and 1706 follow-up visits were recorded, with PD being the primary diagnostic category at the Philadelphia PADRECC (D. McHale, personal communication, May 6, 2008).

The Penn PD & MDC provides comprehensive care to patients with PD and related disorders. The Center is part of the Penn Comprehensive Neuroscience Center and is the sister university site for the PVAMC PADRECC. Recognized by the National Parkinson Foundation as one of its 45 worldwide Centers of Excellence, the PD & MDC is one of the largest of its kind in the country, providing care to approximately 2,000 patients each year. The PD&MDC and the Center for Neurodegenerative Disease Research at Penn were recently named the newest Morris K. Udall Center of Excellence for PD Research by the National Institute of Neurological Disorders and Stroke.

The recruitment of study participants from two large movement disorder centers allowed access to the relevant population, opportunity to assess pain in patients with PD symptoms managed by a neurological movement disorder specialist, and comprehensive health records. For patients similar to this population, findings can be generalized across clinical settings. The limited representation of minorities was a limitation.

Inclusion criteria

Participants were English speakers, diagnosed with idiopathic PD, rated pain as a "two" or greater on the average pain question of the BPI, and responded independently to questions in an interview format without proxy participation. Participants agreed to take part in a study procedure lasting up to two hours.

Exclusion criteria

Patients diagnosed with Parkinson-plus or related movement disorders, indicating "no pain" or a pain score of "one" on the BPI average pain question, unable to speak or read English, or requiring caregiver proxy participation due to marked cognitive impairment were excluded from the study.

Sample Size

For specific aim no. 1, the sample size was estimated at 109 participants using a conservative approach for finding relationships between pain severity and categorical pain variables (*pain stimuli* and *receptor system*). The assumptions used a maximum of three categories for any variable, an alpha of 0.05 and 80% power, to detect a moderate effect size of 0.10 using a one-way analysis of variance (ANOVA) model.

For aim no. 2, sample size calculations estimated the need for 85 participants for a magnitude of correlations set at a minimum of 0.3 among variables for the *emotional-affective system* (depression and affective quality characteristics), *cognitive processes* (attention and beliefs), *perceptual-sensory system* (pain severity and sensory quality characteristics), and *pain behavioral response system* (interference), with alpha set at 0.05 and power of 80%. In order to obtain an adequate sample size to address both specific aims and strive for representation of participants with mild, (n = 50, BPI average pain 2 - 4), moderate (n = 50, BPI average pain 5 - 6),

and severe pain (n = 25, BPI average pain > 7), 125 eligible subjects were required for the study.

Study Procedures

Sample Recruitment and Informed Consent

The PI provided clinical staff with a study advertisement flyer that was approved by the Philadelphia VA Medical Center Institution Review Board (IRB) or the Penn IRB to give to potential study participants. Clinicians informed potential PD patients about the study and directed them to contact the PI. In addition, the flyer announcing the study was distributed to PD patients and local PD support group leaders via mass mailing or in person. Flyers were posted in the waiting rooms in both movement disorder centers. The PI was available during clinic times to meet with potential study participants, and answer questions. Several potential study participants left messages on the PIs answering service at the PADRECC.

All patients arriving for routine follow-up appointments were asked to rate their pain on the BPI sensory pain subscale. Individuals indicating a minimum of *two* on the average BPI pain item were invited to learn more about the study. For individuals meeting all inclusion criteria and interested in joining the study, the PI reviewed the consent and Health Insurance Portability and Accountability Act (HIPAA), prior to initiating study procedures. In addition, VA participants were asked three questions to determine their understanding of study procedures. VA informed consent procedure included a witness for the participants consent signature.

After the consent form was reviewed, potential study participants could ask any questions about the study and all procedures. A copy of the consent and HIPAA form were provided to each participant at the conclusion of the interview. The originals are retained and stored in a locked cabinet in the PI's office at the VA in the PADRECC (room A448). All consent forms are stored separately from case report forms. If a potential participant was unable or unwilling to sign the consent and HIPAA form and comply with recruitment procedures, they were not enrolled in the study.

Administration of questionnaires and compensation

Once the patient was enrolled, the PI met with the participant in a private office or exam room to complete the interview. A study folder was prepared with the following materials:

approved consent, HIPAA form, three-item screening tool (VA only), and case report forms. Current medications and all medical diagnoses were retrieved from the participant's medical record. Demographics were collected at the time of interview and included age, ethnicity, marital status, education, employment status, height, weight, and body mass index. Six questionnaires were administered: 1) the Unified Parkinson's Disease Rating Scale (UPDRS), 2) the Geriatric Depression Scale Short Form (GDS-SF), 3) the Montreal Cognitive Assessment, 4) the Pain Catastrophizing Scale, 5) The Brief Pain Inventory Short Form and, 6) the Short-Form McGill Pain Questionnaire. Each questionnaire was administered in an interview format to limit fatigue due to PD symptoms such as tremor, rigidity, and bradykinesia. Data from interviews were entered on case report forms for scanning.

The GDS-SF and UPDRS are routinely obtained during clinical visits. If these data had been collected in the past seven days, the existing data from the medical record were entered onto the case report forms. Otherwise, the GDS-SF and UPDRS were collected at the time of the study interview. Participants could withdraw from the study at any time, for any reason, with no negative consequences for their medical care and no penalties for early termination. The PI was sensitive to the need for varying amounts of time for each interview.

At the completion of the study visit, the participant completed a compensation form in order to disperse a check for \$30.00 by mail. Compensation was estimated to be reasonable given the time required to complete all questionnaires and travel time and expenses to and from the movement disorder center (Dickert, Emanuel, & Grady, 2002). Eligibility to receive study compensation was clearly explained in the consent procedure.

Each participant was assigned a five-digit identification number from a random table of numbers from <http://www.randomizer.org/form.htm>. The five-digit identifier was entered at the top of each case report form (CRF). Data were entered directly onto the scanable CRFs, developed with Cardiff TELEform® technology, at the time of the interview. The CRFs were scanned into an Excel spreadsheet on a computer located in the PADRECC. Scanned data is stored on the PADRECC server, which is pass code protected for security of information. No PHI, as defined by Safe Harbor De-Identification (45 CFR 164.514(b)(2)), were entered into CRFs. No participants

were over the age of 89, which negated the need to examine cases for identifiable information in the data set. An electronic Excel spreadsheet with the participant name and corresponding unique five-digit identifier is maintained on the PADRECC server and only accessible to the PI.

Study Measures

Introduction

The following section contains a description of measures to ascertain six components of pain based on the modified model by Rugh's (1987) *Psychological Components of Pain*: 1) *pain stimulus*, 2) *receptor system*, 3) *emotional-affective system*, 4) *cognitive processes*, 5) *perceptual-sensory system*, and 6) *pain behavior response system*. *Pain stimulus* was measured by ascertaining symptoms of PD and co-morbid disease states on a standard neurological scale. The *receptor system*, representing neuropathic, nociceptive, or mixed pain, was measured through a modified International Association for the Study of Pain classification. The *emotional-affective system* was measured by a standard depression scale and an affective quality of pain scale. A brief cognitive screen and instrument for pain catastrophizing was used as a measure of *cognitive processes*, incorporating beliefs and attention to pain. The *perceptual-sensory system*, representing severity and sensory quality of pain, was measured through standard pain scales. Lastly, the *pain behavioral response system* was measured through an assessment of interference from a standard pain scale.

Variables for Pain Stimulus: Injury or disease

Pain stimulus was measured using the Unified Parkinson's Disease Rating Scale (UPDRS) and dividing the sample into two clinical PD subtypes (Jankovic et al., 1990). The UPDRS is the current gold standard for measuring PD symptoms in clinical trials (Fahn, Elton, & Members of The UPDRS Development Committee, 1987; Goetz, LeWitt, & Weidenman, 2003; Goetz & Stebbins, 2004). Although some limitations exist concerning reliability and validity data of the UPDRS, a newer version currently under development by the Movement Disorder Society is not available at this time (Goetz et al., 2007; Goetz, Poewe et al., 2003).

The origin of the UPDRS is the *Columbia Scale* tested on 70 adults, mean age 64.8 (± 10.8) years, and followed in a study at an ambulatory movement disorder center (Montgomery,

Reynolds, & Warren, 1985). Subsequently, a committee was formed to refine and publish the study scale as a standard measure for PD clinical trials (Fahn, et al., 1987). The current UPDRS has five subscales: Part I – Mentation, Behavior, and Mood (4 items); Part II – Activities of Daily Living (13 items); Part III - Motor Examination (14 items); Part IV - Motor Complications (11 items); and Part V – the one item Schwab and England (SE) Activity of Daily Living Scale. All items in the first three subscales are rated on a five-point Likert scale from zero to four. Scoring is not consistent, but generally follows the pattern: 0 = normal, 1 = slight, 2 = mild, 3 = moderate, and 4 = severe (Fahn, et al.). Part IV of the UPDRS is the single item Modified Hoehn and Yahr (HY) Staging Scale and is a standard for reporting stage of disease. HY stage of disease is rated as: 0 = No signs of disease; 1 = Unilateral disease; 1.5 = Unilateral plus axial involvement; 2 = Bilateral disease without impairment of balance; 2.5 = Mild bilateral disease, with recovery on pull test; 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. Higher scores reflect a higher severity of disease (Goetz et al., 2004). Part V of the UPDRS is composed of the SE Activity of Daily Living Scale and is a standard measure in clinical trials reporting activity of daily living in PD. This one-item subscale is scored in 10-point increments from 100% (complete independence) to 0% (vegetative function) (Fahn et al.). Estimated time to complete the full UPDRS is 15 minutes.

Reliability for four UPDRS subscales is adequate with a Cronbach's alpha of .79 (UPDRS I), .92 (UPDRS II & III), and .83 (UPDRS IV) (Martinez-Martin & Forjaz, 2006). Construct validity was established for the Short Parkinson's Evaluation Scale (SPES) and the UPDRS in a study of 59 subjects. Spearman coefficients demonstrated good correlation between activities of daily living (ADL) (.88) and motor exam (.90) subscales (Martignoni, Franchignoni, Pasetti, Ferriero, & Picco, 2003). Validity of UPDRS subscales I, II, and III was adequate with factor analysis. Some overlap in item content suggested that items 16, 17, 20, 21, 40, 41, and 42 might be eliminated without compromising validity (Martinez-Martin & Forjaz). The UPDRS, including the HY and SE, are acceptable and meet scaling assumptions (Martinez-Martin & Forjaz).

The formula presented by Jankovic et al. (1990) divides PD into tremor-dominant, postural-instability-gait-disorder (PIGD), and indeterminate PD subtypes (Burn et al., 2006). The average global tremor score was calculated from the mean sum of the baseline tremor score (UPDRS II, item 16) and tremor scores (UPDRS III, items 20-21) for face, right hand, left hand, right foot and left foot and action tremor, right and left. Mean PIGD score was calculated from the mean of UPDRS items for falling (item 13), freezing (item 14), walking (item 15), gait (item 28) and postural stability (item 29). Patients were categorized as having tremor-dominant PD if the ratio of the mean tremor score to the mean PIGD score was ≥ 1.5 or categorized as PIGD if the ratio was ≤ 1.0 . Cases with a ratio between 1.1 and 1.4 were coded as indeterminate PD subtype, as their symptoms had not differentiated into tremor or PIGD specific. Co-morbid diseases were identified from the medical record and listed on the case report forms.

Variable for Receptor System: Classification of pain

A major limitation in the study of pain in PD is the absence of a consistent classification system based on current pain literature and science. To address this shortcoming, pain was classified using the International Association for the Study of Pain (IASP) five axis classification system, modified by the PI (Merskey & Bogduk, 1994; Turk & Rudy, 1987). The IASP structure provided measurement for the *receptor system* utilizing a modified Axis II that describes pain as nociceptive or neuropathic pain, and Axis V by defining etiology according to Lee's classification of pain in PD (M. A. Lee et al., 2006). The original IASP Axis V has been replaced with five items: 1) pain related to idiopathic PD; 2) treatment related pain; 3) pain indirectly related to PD; 4) pain unrelated to PD; and 5) other or multiple causes of pain (M. A. Lee et al.). Lee's survey of 123 patients with PD (Mean age 75.4 years) was the first to demonstrate that PD related pain and non-PD related pain often coexist, but are differentiated as separate pain symptoms. The sample described 285 distinct painful symptoms of which 94.7% were classified as nociceptive pain and only 5.3% were classified as neuropathic pain syndromes (M. A. Lee et al.). Lee's classification system is not validated, but served as a method to organize *receptor system* variables.

Variables for Emotional-Affective and Perceptual-Sensory System

Models incorporating psychosocial variables, as important aspects of the pain experience, have not been adequately developed in the PD pain literature. To fill this void, the *emotional-affective system* measured depression and verbal descriptors of affective quality of pain. The *perceptual-sensory system* was measured by sensory verbal descriptors and severity of pain.

The Geriatric Depression Scale – Short Form (GDS-SF). The GDS-SF was used to measure depression and has been frequently utilized in PD protocols (Meara, Mitchelmore, & Hobson, 1999; Schrag et al., 2007; Weintraub, Oehlberg, Katz, & Stern, 2006; Weintraub, Saboe, & Stern, 2007; Weintraub, Xie, Karlawish, & Siderowf, 2007). The original 30 item GDS (Yesavage et al., 1983) served as the basis for development of the 15-item GDS-SF (Sheikh & Yesavage, 1986). To determine if the GDS-SF could differentiate depressed from non-depressed older adults, Sheikh and Yesavage administered both the original long version and the short form of the GDS to 18 community dwelling older adults and 17 elders meeting DSM-III criteria for depression. There was a high correlation between both versions of the GDS ($r = .84, p < .001$) suggesting that the GDS-SF can be used as a brief screen for depression in older adults (Sheikh & Yesavage).

The GDS-SF is a 15-item self-rated questionnaire. Each question is answered as *yes* or *no* and has a possible score of zero or one. The total scale score is calculated with the following cutoffs for scoring: 0 to 4, normal; 5 to 8, mild; 8 to 11, moderate; and 12 to 15, severe (Sheikh & Yesavage, 1986). Estimated time to complete is 10 minutes. Construct validity for the GDS-SF was established in a study of 116 older adults followed in a psychiatric clinic. The Pearson's correlation coefficient for the GDS-SF and the Montgomery Asberg Depression Rating Scale was high ($r = .78$) (Herrmann et al., 1996). Criterion validity GDS-SF cutoff scores of five or six, out of a total score of 15, demonstrated a sensitivity of 85% and specificity of 74% for detection of depression (Herrmann et al.). Validity was adequate in a comparison between the Hamilton Depression Rating Scale and the GDS-SF in patients with PD (Weintraub et al., 2006). Reliability was established with internal consistency of the GDS-SF with a Cronbach's alpha of 0.75

(Friedman, Heisel, & Delavan, 2005). Psychometric properties of the GDS-SF were established in community dwelling older adults with functional impairment (Friedman et al.). Sensitivity of the GDS-SF, to screen for depression, was demonstrated in a study of 148 PD patients in an ambulatory care setting, mean age 72 years (± 8.5), range 40-90 (Weintraub et al., 2006).

Short Form - McGill Pain Questionnaire (SF-MPQ). The SF-MPQ is a widely used measure of pain in clinical research, developed to provide a brief version (15-item word list), self-reported, multidimensional data collection instrument (Melzack, 1987; Melzack & Katz, 2006). The original long form MPQ, containing 78 word descriptors, was based on ratings of 102 pain descriptors by physicians, patients, and university students, resulted in three subscales: sensory, affective and evaluative (Melzack & Torgerson, 1971). Testing for the SF-MPQ included comparisons between the long form MPQ and SF-MPQ in postoperative patients ($n = 40$), obstetrical patients ($n = 20$), dental patients ($n = 31$), and patients with musculoskeletal pain ($n = 10$), to identify descriptors that demonstrated sensitivity to change with pain treatment (Melzack, 1987).

Further testing of the SF-MPQ yielded two subscales, the sensory and affective, and consisted of 15 adjectives derived from the original MPQ version (Melzack, 1975). Each descriptor is scored on a four-point Likert scale: 0 = none, 1 = mild, 2 = moderate, and 3 = severe (Melzack & Katz, 2006). Several published studies on PD and pain have utilized the MPQ; however, none have reported reliability or validity data (Carroll et al., 2004; Goetz et al., 1986; Massetani et al., 1989; Pacchetti et al., 1995; Starkstein et al., 1991). Estimated time to complete the SF-MPQ is five minutes. Gagliese and Melzack (2003) conclude that both the original and short form of the MPQ are appropriate for use with older adults, and that elders demonstrate differences in the quality of pain, but no difference in the severity of pain, as compared to younger adults.

Reliability of the SF-MPQ was established with internal consistency Cronbach's alpha ranging from 0.67 and 0.87 in research with dental patients and post-operative patients (Melzack, 1987). Test-retest reliability was strong for the SF-MPQ and subscales (Melzack & Katz, 2006). Content validity for the full SF-MPQ was reported in adult patients with post-operative pain using

words for sensory and affective qualities (McDonald & Weiskopf, 2001). The SF-MPQ is sensitive to change in studies of interventions for pain, and discriminates between types of pain syndromes (Melzack & Katz).

Factor analysis supports construct validity for two separate domains of affective and sensory qualities of pain (Melzack & Katz, 2006). The Affective subscale of the SF-MPQ measured the affective quality of pain. Four word descriptors of *tiring-exhausting*, *sickening*, *fearful*, and *punishing-cruel* represent the Affective subscale and were scored on a four-point Likert scale and summed to calculate a score for the affective quality of pain (Melzack, 1987). Internal consistency for the Affective subscale was reported with a Cronbach's alpha of 0.71 (Turk, Rudy, & Salovey, 1985). Construct validity of the affective dimension of the MPQ was demonstrated in a study of 68 patients followed in an ambulatory pain center, comparing the subscale to the Sickness Impact Profile and the Brief Symptom Inventory (Kremer & Atkinson, 1981).

The SF-MPQ Sensory subscale measured the variable for sensory quality in the *perceptual-sensory system*. It consists of 11 word descriptors: throbbing, shooting, stabbing, sharp, cramping, gnawing, hot burning, aching, heavy, tender, and splitting. Each descriptor is scored on a four-point Likert scale and then summed to obtain the subscale score (Melzack & Katz, 2006). Concurrent validity for the Sensory subscale was determined by comparing results of the MPQ and the Geriatric Pain Measure (GPM) using Pearson's r correlations between subscale scores. Correlations between the sensory and GPM pain severity subscales demonstrated statistical significance ($r = .53, p < .000$) (Ferrell, Stein, & Beck, 2000). The Sensory subscale for the SF-MPQ has adequate internal consistency with a Cronbach's alpha of 0.78 (Turk et al., 1985).

Variable for Cognitive Processes: Attention and Beliefs

To measure variables for attention to pain and beliefs regarding pain, the Montreal Cognitive Assessment (MoCA) and the Pain Catastrophizing Scale (PCS) were chosen. Both of these measures capture the conceptual domains for attention and beliefs as displayed in the Rugh (1987) Model.

Montreal Cognitive Assessment (MoCA). The MoCA (Nasreddine et al., 2005) is designed as a brief screen for mild cognitive impairment in individuals scoring in the normal range on the Mini Mental State Exam (MMSE) (Folstein et al., 1975). Nasreddine et al. administered the MoCA and the MMSE to older adult controls (n = 90, mean age 72.84), ambulatory care patients meeting criteria for mild cognitive impairment (n = 94, mean age 75.19), and to patients diagnosed with Alzheimer's disease (n = 93, mean age 76.72). The MMSE demonstrated an 18% accuracy to detect mild cognitive impairment, using a 26 out of 30 point cutoff score; however, the MoCA identified 90% of individuals with mild cognitive impairment. The MoCA contains eight cognitive domains: attention, executive function, memory, language, visuoconstructional skills, abstract thinking, calculations, and orientation. Approximate time to complete is 10 to 15 minutes, with scores ranging from zero to 30, with 26 or above being normal (Nasreddine, et al.).

Nasreddine et al. (2005) reported internal consistency reliability of the MoCA as excellent with a Cronbach's alpha = 0.83. Test-retest reliability was excellent, with correlation coefficient = 0.92 in comparison test scores in patients with mild cognitive impairment and Alzheimer's disease at two points in time (Nasreddine et al.). Validity of the concept of cognitive impairment is consistent with high correlation (r=.87) between the MoCA and the MMSE. However, the MoCA is more sensitive to a range of mild cognitive impairment (Nasreddine et al.).

Two published studies compared the MoCA with the MMSE in detecting mild cognitive impairment. The first study administered the MoCA and the MMSE to three groups of patients: patients meeting dementia criteria (n = 32), patients meeting criteria for mild cognitive impairment (n = 23), and a control group followed in a memory disorder clinic (n = 12) (Smith, Gildeh, & Holmes, 2007). Findings showed the MoCA to be superior to the MMSE in detecting patients with mild cognitive impairment (83%), compared to an MMSE with the cut off score of 26 (17%). Sensitivity to detection of dementia was 94% for the MoCA and 25% for the MMSE. Thirty-five percent of individuals scoring below 26 on the MoCA at baseline went on to develop dementia in six months (Smith, et al.). The only published study utilizing the MoCA to assess cognitive impairment in PD demonstrated the instrument to be more sensitive than the MMSE in the identification of a continuum of cognitive impairment (Zadikoff et al., 2008). Scores of 99 PD

patients were compared using the MMSE and MoCA, showing a ceiling effect score with the MMSE. The range of scores for the MMSE (16-30, \pm 2.55) were narrow and the MoCA were more broad (7-30, \pm 4.26), indicating greater sensitivity to mild cognitive deficits in PD (Zadikoff et al.).

The Pain Catastrophizing Scale (PCS). The PCS (Sullivan, Thorn et al., 2001), designed to elicit thoughts and feelings regarding the pain experience, was used to measure beliefs regarding pain. Scale development for the PCS was conducted with undergraduate students (Sullivan & Bishop, 1995), therefore limiting the ability to apply psychometric testing to other populations. Validity and reliability of the PCS has not been published for patients with PD; however, a study of community dwelling adults (n = 215) and outpatients (n = 60) demonstrated psychometric soundness (Osman et al., 2000).

Composed of 13 statements, the PCS is scored on a five-point Likert scale, with items on thoughts and feelings about pain rated as: 0 = not at all, 1 = to a slight degree, 2 = to a moderate degree, 3 = to a great deal, and 4 = all the time (Sullivan et al., 1995). Three distinct subscales included rumination, magnification, and helplessness (Osman et al., 2000; Osman et al., 1997). Total scores are calculated by summing all items with a score ranging from zero to 52. The PCS has been used in numerous research protocols on pain in patient populations, laboratory induced pain, and community dwelling adults (Sullivan, Thorn et al., 2001). Estimated time to complete the PCS is five minutes (Sullivan, 2004).

Reliability was reported as excellent with a Cronbach's alpha of .92 (outpatient sample n = 60) and .95 (community sample, n = 215) (Osman et al., 2000). As discussed in chapter two, an oblique factor analysis confirmed construct validity of the PCS for the measurement of catastrophizing pain as a single construct, as well as identifying three dimensions of catastrophizing: rumination, magnification, and helplessness (Osman et al.). Concurrent validity for the PCS was provided in comparing subscales of the Positive and Negative Affect Schedule Scales (PANAS) with the PCS, which has been the standard scale for validity testing in other studies (Sullivan et al., 1995). Results suggest that moderate levels of catastrophizing were positively related to negative affect ($r = .31, p < .001$) and negatively related to positive affect ($r = .30, p < .001$), suggesting the PCS and the PANAS measure different constructs and do not

support prior psychometric research (Osman et al.). The total PCS score, however, significantly correlates with measures of pain severity ($r = .51, p < .001$) and measures of pain interference ($r = .57, p < .001$) (Osman et al.).

Variables for Perceptual-Sensory System and Pain Behavior Response

Pain severity and behavior was measured with the Brief Pain Inventory - Short Form (BPI-SF). The BPI-SF assesses both the *perceptual-sensory system* and the *pain behavior response system* of the Rugh (1987) Model.

The Brief Pain Inventory - Short Form (BPI-SF): The original BPI was called the Wisconsin Pain Inventory, and was modeled after the MPQ to assess cancer pain (Daut, Cleeland, & Flanery, 1983). Subsequent psychometric analyses and testing have produced a brief version of the BPI, which has gained widespread acceptance in pain research as the “gold standard” for assessing patients with both cancer-related and noncancer pain (Keller et al., 2004; Tan et al., 2004). Tan et al. (2004) tested the BPI-SF in a study of 440 pain clinic patients (mean age 54.9 years, range 21-85 years) at a Veteran’s Affairs Medical Center and found it to be reliable and valid. Estimated time to complete the BPI-SF is five minutes, and the tool can be administered in either a self-report or an interview format.

The scale is composed of 15 items with a factor analysis that supports two subscales, pain severity and pain interference (Tan et al., 2004), as well as acceptable reliability and validity data for both subscales. The subscale for pain severity consists of four items rated from 0 = “no pain” to 10 = “worst pain”. The arithmetic mean represents pain severity. The pain severity subscale has a range of zero to 40 (Fortner et al., 2003). Reliability and validity were reported in a study of 250 patients with arthritis or low back pain (Keller et al., 2004). Construct validity for the BPI severity subscale was established with satisfactory correlational coefficients showing a strong relationship with the SF-36 Bodily Pain Scale and the Health Assessment Questionnaire (Keller et al., 2004). Internal consistency of the pain severity subscale was supported with a Cronbach’s alpha of 0.89 (Keller et al.) and 0.85 by Tan et al. (2004).

Pain behavior response was measured using the BPI-SF subscale for pain interference, which consists of seven items rated from zero to 10. Pain interference is assessed based on

activity, mood, ambulation, work, relationships, sleep, and enjoyment of life. The subscale was scored by taking the mean score for each of the seven items for pain interference, mean range of zero to 10. Validity and reliability of the BPI Pain interference subscale was reported in a study examining 133 adults with osteoarthritis (V. S. Williams et al., 2006). Internal consistency of the pain interference subscale was demonstrated by a Cronbach's alpha of .89 (V. S. Williams et al.). Concurrent construct validity was supported with acceptable Pearson's Product Moment correlations estimated associations between pain interference measures and selected items on the Western Ontario McMaster Universities Osteoarthritis Index (r range from .39 to 0.64). Scores were positive and statistically significant, indicating concurrent validity of the Pain Interference subscale for the BPI (V. S. Williams et al.). Test-retest was supported with an Intraclass Correlation Coefficient of 0.81 (95% CI: 0.68- 0.90) in stable osteoarthritis patients (Williams et al.).

Human Subjects Consideration

Data monitoring and data safety. Data collection, scanning, storage, access, and statistical analysis were managed and monitored by the PI. As described earlier, participants were assigned five digit random numbers for identification codes. Identification codes were included on case report forms and used in the data set to identify cases for statistical analysis. A separate Excel file has been maintained by the PI to link five digit identifiers to participants' names. Only the PI has access to the electronic file with participant names and five digit codes. Case report forms continue to be stored separately from consent forms to limit identification of study participants. All consent forms, HIPAA forms, three question quizzes (VA only), and case report forms are locked in a file cabinet in the PI's office in the PADRECC (room A448). All electronic data are stored on the PADRECC *Z Drive*, which is housed in the Philadelphia VA Medical Center on a Dell Optiplex GX240, Intel (R), Pentium (R) 4 CPU. The database is supported by Microsoft Office Excel 2003. The PADRECC *Z Drive* is contained on a secured server, is password protected, and is behind a firewall.

Data cleaning and verification were completed by the PI. Scanned case report forms were reviewed for accuracy against the excel database and the database was corrected for

inaccuracies. Prior to data analysis, a random sample of 20% of the original data from the questionnaires and demographic forms was reviewed for accuracy. No identifiable data were contained in the final data set prior to statistical analysis. All electronic records, case report forms, HIPAA forms, and three-item quiz associated with this protocol are stored indefinitely in accordance with Veterans Hospital Administration (VHA) Records Control Schedule. Data analysis took place in the PADRECC and the Center for Health Equity Research and Promotion (CHERP) at the Philadelphia VA Medical Center.

Safety plan. Protocol deviations, adverse events, serious adverse events, and breaches of confidentiality were to be reported to the Philadelphia VA IRB and the IRB of the University of Pennsylvania according to established protocols and timelines. There were no protocol deviations, adverse events, serious adverse events, or breaches of confidentiality in the course of this study. Study participants screened with the Geriatric Depression Scale and found to be clinically depressed were referred to their clinician for follow up services. The only potential risk from participating in the study was possible fatigue from completing the interview and emotional stress associated with discussing painful symptoms. Study participants were given an opportunity for a break during data collection to minimize fatigue and emotional distress. Item burden was considered acceptable based on the interview format for data collection. Patients found to have untreated pain were referred to their provider for evaluation. There was no clear benefit for study participants in this protocol other than adding to knowledge regarding pain in PD. Participation in this protocol was voluntary and the study participant could withdraw at any time.

Statistical Analysis

Initial data analyses were conducted at the PADRECC and complex analyses were performed at the CHERP at the Philadelphia VA Medical Center by the center's statistician, Anne Canamucio, PhD. Analyses at the PADRECC utilized SPSS Software Version 17.0 (Chicago, Illinois), whereas SAS Statistical Software Version 9.2 (SAS Institute Inc., Cary, NC) was used at the CHERP. Alpha (p-value) was set at 0.05 for statistical significance.

All data were summarized using descriptive statistics. Measures of central tendencies (e.g., mean, median, mode, range, and standard deviations) were calculated for all continuous

level variables. Categorical variables were reported as frequencies and percentages. When appropriate, graphical displays of continuous level data were presented in histograms and transformations to normality as necessary. Both parametric for continuous level data and nonparametric statistics for nonnormally distributed data, ordinal or nominal data, were used for the statistical analyses.

For aim no. 1, frequencies were used to describe pain types (nociceptive or neuropathic pain) and etiology of pain related to PD. Three independent groups were identified for PD subtypes (postural-instability-gait-disorder (PIGD), tremor-dominant, and indeterminate) that may modulate pain severity (mild = average BPI pain score 2 - 4, moderate = average BPI pain score 5 - 6, and severe = average BPI pain score \geq 7). Composite ratings for tremor dominant, PIGD, and indeterminate PD subtypes were correlated with pain severity categories (mild, moderate, and severe pain) using the Spearman's rho correlation. Pain severity groupings were compared using ANOVA across continuous or ordinal variables.

For aim no. 2, correlations and comparisons of participant-reported outcomes were used to identify relationships and differences between and among the *emotional-affective system* (depression and affective quality characteristics), *cognitive processes* (attention and beliefs), *perceptual-sensory system* (pain severity and sensory quality characteristics), and the *pain behavioral response system* (interference) in patients with PD. Pearson's correlation coefficients were used to assess the magnitude of relationships and ANOVA for differences between average pain, as a continuous variable, and for continuous variables for depression, attention, pain interference, beliefs, pain affective quality, and pain sensory quality. Linear regression analyses were used and assumed pain interference as the dependent variable, as identified in the Rugh (1987) Model; independent variables were depression, pain affective quality, attention, beliefs, pain severity, and pain sensory quality.

CHAPTER 4

Results

Introduction

Results for all descriptive and inferential statistics are provided in this chapter, along with the findings, which are arranged according to the research questions. Additional data are reported for the sample itself, in particular disease-related characteristics. When appropriate, the results are displayed in tables and figures.

Recruitment

Recruitment began on October 24, 2008, and all study participants were enrolled by September 15, 2009. A total of 286 potential participants were screened for eligibility, and of these, 190 were approached. A final sample of 125 eligible and willing research participants were consented, enrolled, and completed the study (43% recruitment rate). All participant study data were gathered over 93 days, with 508 hours spent in the clinical setting devoted to recruitment. Table 2 illustrates the recruitment numbers and participant status at both the Penn PD & MDC and at the Philadelphia VAMC PADRECC study sites. The average pain question from the BPI-SF was used to define inclusion criteria for the study, and served as the primary measure for pain severity. Participants needed to rate average pain in the last 24 hours as ≥ 2 to be enrolled.

Table 2

Recruitment Data Screening

Recruitment status	Pain<2	Pain \geq 2 CNS	Pain \geq 2 Declined	Other NR	Pain \geq 2 Recruited	Total
Penn PD & MDC	65	53	6	4	96	224
PADRECC	21	5	1	6	29	62
Total	86	58	7	10	125	286

Pain < 2: Participant rated average pain as zero or one, did not meet criteria

Pain \geq 2 CNS: Pain rated as two or greater but individual could not stay for interview

Pain \geq 2 Declined: Pain rated as two or greater but individual declined to participate

Other NR: Not Recruited (dementia, not idiopathic PD, non-English speaking)

Pain \geq 2 Recruited: Average pain rated as two or greater, recruited into study

Research Questions

Two research questions formed the basis for the study and were guided by the specific aims for the investigation, the Rugh (1987) Model of Pain, and existing literature. All statistical analyses were performed on participant-specific demographic and disease variables and participant outcome measures and instruments used in the study.

1. What are the relationships and effects of Parkinson's disease (e.g., tremor-dominant, postural-instability-gait-difficulty, and indeterminate subtypes), and pain-related pain types (nociceptive, neuropathic, and mixed) variables on participant-reported pain severity?
2. What are the relationships among the *emotional-affective system* (depression and affective quality characteristics), *cognitive processes* (attention and beliefs), *perceptual-sensory system* (pain severity and sensory quality characteristics), and *pain behavioral response system* (interference) in patients with Parkinson's disease?

Sample Characteristics

Sample Characteristics – All Participants

Demographic characteristics are shown in Tables 3 and 4, with means, standard deviations and minimum and maximum values reported. The sample was well educated, predominately Caucasian (97%) and male (70%) with a mean age of 67 (± 0.7) years. Most participants were married (76%), lived with family members (69.6%), and had retired from active employment (55%). On average, the group had experienced PD symptoms for approximately 106 months, which was similar to the duration of experiencing painful symptoms, 105 months. As a group, participants mean body mass index (BMI) fell in the overweight category. The definitions used for BMI classifications were: normal (BMI < 25 kg/m²), overweight (BMI between 25 kg/m² and 30 kg/m²), and obese (BMI \geq 30 kg/m²) (Marcus, 2004).

Table 3

Continuous Demographic Characteristics (N=125)

	Mean	Standard Deviation	Minimum	Median	Maximum
Age (Years)	66.83	0.7	43	67.00	85.0
Education (Years)	15.70	2.8	8	16.00	24.0
Time from PD Diagnosis (Months)	85.06	69.8	12	72.00	300.0
Time from PD Symptoms (Months)	106.66	77.9	12	96.00	372.0
Duration of Pain (Months)	105.02	108.5	1	60.00	564.0
Body Mass Index (BMI)	27.69	5.1	19	27.26	45.9

The formula published by Jankovic et al. (1990) to categorize PD patients into three subtypes, tremor-dominant, PIGD, or indeterminate subtypes, was presented in chapter 3 and is derived from data collected on the Unified Parkinson's Disease Rating Scale (Fahn et al., 1987). Interestingly, the sample consisted primarily of individuals with PIGD subtype (84.8%) as compared to the tremor-dominant subtype (9.6%). Seven cases (5.6%) did not fit into either subtypes and are categorized as indeterminate, as the cases had not differentiated clearly into a tremor or PIGD subtype (Burn et al., 2006) (Table 5).

Table 4

Categorical Demographic Characteristics (N=125)

	Category	Frequency	Percent
Sex	Male	88	70.4
	Female	37	29.6
Ethnicity	Caucasian	121	96.8
	African American	3	2.4
	Asian	1	0.8
Residence	Private alone	32	25.6
	Private w family	87	69.6
	Nursing home	2	1.6
	Retirement Community	1	0.8
	Assisted Living	2	1.6
Marital Status	Single	7	5.6
	Married	95	76.0
	Divorced	15	12.0
	Widow(er)	8	6.4
Employment	Retired	69	55.2
	Working Full-time	22	17.6
	Working Part-time	14	11.2
	Disability	17	13.6
	Unemployed	3	2.4

Table 5

Clinical PD Subtypes: Tremor Dominant, PIGD, and Indeterminate (N=125)

	Frequency	Percent	Cumulative Percent
Tremor Dominant	12	9.6	9.6
PIGD Dominant	106	84.8	94.4
Indeterminate	7	5.6	100.0

Stage of disease was described utilizing the Hohen and Yahr (HY) scale (Table 6). Most participants were rated at stage 2.5, defined as mild bilateral PD with recovery on pull test (33.6%), or stage 4.0, defined as severe disability yet still able to walk or stand unassisted (36%). Over half the sample (n = 73, 58.4%) were rated at HY of 3.0 or greater, demonstrating a sample of individuals with moderate to advanced disease.

Table 6

Hoehn and Yahr (HY) Stage of Parkinson's Disease (N=125)

	Frequency	Percent	Cumulative Percent
1.5 = Unilateral plus axial	3	2.4	2.4
2.0 = Bilateral no balance impairment	7	5.6	8.0
2.5 = Mild bilateral	42	33.6	41.6
3.0 = Mild to moderate bilateral	20	16.0	57.6
4.0 = Severe	45	36.0	93.6
5.0 = Very severe	8	6.4	100.0

Functional limitations from PD were rated using the Schwab and England (SE) Activities of Daily Living (ADL) scale (Table 7). Participants' SE scores ranged from complete independence to needing help with ADLs, with most of the sample (n=83; 66%) completely independent. Individuals scoring 90% on the SE (n=44, 39%) were independent in ADLs, but reported awareness of difficulty in completing daily tasks.

Table 7

Schwab and England Activities of Daily Living

	Frequency	Percent	Cumulative Percent
100% Completely independent	34	27.2	27.4
90% Completely independent, aware of difficulty	49	39.2	66.9
80% Independent, takes twice as long	18	14.4	81.5
70% Not completely independent	11	8.8	90.3
60% Some dependency	4	3.2	93.5
50% More dependent	7	5.6	99.2
30% Much help needed	1	0.8	100.0

Summary of population under study. Participants were predominately overweight, well educated, older, married, Caucasian, males who were retired from active employment. On average, participants had experienced PD symptoms and pain for approximately nine years. Parkinson symptoms were moderate to advanced with over half of the sample at HY stage 3.0 or greater, yet the group was highly functional in measures of activities of daily living. The vast majority of participants were categorized as PIGD PD subtype, as compared to the tremor predominant PD clinical subtype.

Descriptions of Pain

The Brief Pain Inventory-Short Form (BPI-SF) and the modified International Association for the Study of Pain (IASP) scheme for coding chronic pain diagnosis Axis I – V, were used to describe pain severity, locations, and qualities. Pain severity was rated on four scales of the BPI-SF: worst pain in the last 24 hours, least pain in the last 24 hours, average pain in the last 24 hours, and pain right now. Pain levels were scored on a scale from 0, *no pain*, to 10, *worst pain possible*. Pain was categorized as mild (score of 2 to 4), moderate (score 5 to 6), or severe (score ≥ 7). As a group, the mean score of 6.26 (± 2.4), for *worst pain* severity within the last 24 hours, was in the range of moderate pain and mean *average pain* in the last 24 hours approached moderate pain levels (4.5, ± 1.8). The mean pain level at the time of the interview, however, was

mild (2.81, \pm 2.3), with some degree of variability noted in the standard deviation. All measures of central tendency (mean, median, mode and range) appear below in Table 8 for all pain severity dimensions. Average pain was divided into three categories of mild, moderate, and severe to examine the distribution of pain ratings (Table 9). Over half (52%) of the sample described their average daily pain as moderate to severe in the 24 hours prior to the interview.

Table 8

Brief Pain Inventory-Short Form (BPI-SF) Pain Severity (N=125)

	Worst pain	Least Pain	Average Pain	Pain Right Now
Mean	6.26	1.25	4.50	2.81
Median	7.00	1.00	5.00	3.00
Mode	8	0	5	0
Std. Deviation	2.4	1.5	1.8	2.3
Minimum	2	0	2	0
Maximum	10	7	10	10

Table 9

Brief Pain Inventory-Short Form (BPI-SF) Average Pain Groups (N= 125)

	Frequency	Percent	Cumulative Percent
Mild (2-4)	60	48.0	48.0
Moderate (5-6)	46	36.8	84.8
Severe (\geq 7)	19	15.2	100.0

The number of painful locations described by study participants was measured using Axis I of the IASP scheme for coding chronic pain (Merskey & Bogduk, 1994). Almost half (46.4%) the participants reported three or more pain locations, with a mean of 2.46 (\pm 1.07) locations, for a total of 308 pain locations for the entire sample (Table 10). The most common pain locations were the lower limbs, lower back, upper shoulder and upper limbs (Table 11).

Table 10

Total Number of Pain Locations (N = 308 pain locations for N = 125)

Number of locations	Frequency	Percent	Cumulative Percent
1	24	19.2	19.2
2	43	34.4	53.6
3	41	32.8	86.4
4	11	8.8	95.2
5	5	4.0	99.2
6	1	0.8	100.0

Table 11

International Association for the Study of Pain (IASP) Axis I: Pain Location

(N = 125 participants with N = 308 pain locations)

Pain Location IASP Axis I	Frequency	Percent
Face	11	8.8
Cervical	37	29.6
Upper Shoulder and Limbs	70	56.0
Thoracic	9	7.2
Abdominal	6	4.8
Lower Back	84	67.2
Lower Limbs	89	71.2
Anal, Peritoneal of Genital	2	1.6

Table 12

Type of Pain Axis II: Nociceptive or Neuropathic Pain (N = 125 for each pain type, not mutually exclusive)

Pain Type: Axis II	Frequency	Percent
Nociceptive: Somatic - Musculoskeletal	107	85.6
Nociceptive: Visceral	2	1.6
Nociceptive: Other	1	0.8
Neuropathic: Central	0	0.0
Neuropathic: Peripheral	59	47.2
Neuropathic & Nociceptive	43	34.4

During the interview each participant described painful symptoms to the investigator, who would assign pain to a subtype of nociceptive or neuropathic pain itemized in Axis II (Table 12). This method was limited by the participants self-report of pain without physical examination or imaging studies. Study participants (N = 125) described 308 different locations of pain, and several participants indicated symptoms that were consistent with both nociceptive and neuropathic components of pain (n = 43, 34.4%). Most of the pain was characterized as localized spastic, tightness, cramping, stiff, and aching, which is consistent with nociceptive somatic pain of musculoskeletal origin (n = 107 pains, 85.6%). Numerous individuals reported early morning dystonic cramping pain in the lower extremities, which may have been attributed to what is called *wearing off symptoms* of levodopa therapy. Others commented that they had experienced pain from tremors, which had resulted in fatigued, bruised, and achy muscles in the extremities. The existence of comorbid disease states, contributing to the experience of musculoskeletal pain, included arthritis (n = 26, 18%).

Neuropathic peripheral pain, described as numbness, burning, shooting, sharp, tingling, or radiating, was a common category for pain symptoms (n = 59, 47.2%). Such word descriptors reflect the *language of pain* (Melzack & Torgerson, 1971) and are often associated with disease states, such as diabetic neuropathy. None of the participants appeared to have symptoms

consistent with centrally mediated neuropathic pain syndrome, such as thalamic pain (post-stroke pain) or phantom limb pain, based on participant-reported and medical record health histories.

During the interview, participants were asked to describe the temporal quality of their pain experiences as defined by Axis III of the IASP scheme for coding chronic pain diagnoses (Merskey & Bogduk, 1994). Each painful symptom was assigned its own distinct temporal quality based on the categories outlined in Table 13. All participants assigned each of their painful symptoms to one or more temporal characteristics; occurring irregularly (n = 51, 40.8%), occurring regularly (n = 47, 37.6%), continuous without a fluctuating quality (n = 31, 24%), and/or continuous with a fluctuating quality (n = 46, 36.8%).

Table 13

International Association for the Study of Pain (IASP) Axis III: Temporal Characteristics of Pain (N = 125 for each temporal pain characteristic, not mutually exclusive)

Temporal Characteristics of Pain	Frequency	Percent
Single episode, limited duration	1	0.8
Continuous or nearly continuous, non-fluctuating	31	24.8
Continuous or nearly continuous, fluctuating	46	36.8
Reoccurring irregularly	51	40.8
Reoccurring regularly	47	37.6

Axis IV uses the McGill Present Pain Severity scale (Melzack, 1987) requiring that participants select one word, from a list of five words, that best defines their overall pain experience (Table 14). Most participants considered pain to be discomforting (49.6%), while others found pain to be distressing (24.8%) or horrible (11.2%). A considerable number of participants (42%) reported the experience of pain to be distressing, horrible, or excruciating.

Table 14

McGill Present Pain Severity Axis IV: Statement of Pain Severity (N = 125)

Axis IV: Pain Severity	Frequency	Percent
Mild Pain	9	7.2
Discomforting Pain	62	49.6
Distressing Pain	31	24.8
Horrible Pain	14	11.20
Excruciating Pain	8	6.4

Axis V consists of a pain classification taxonomy for PD developed by M. A. Lee et al. (2006). Data for Axis V were collected by querying the participant regarding thoughts on PD and experiences with painful symptoms. Through these interactions with participants, it was possible to categorize each painful symptom into the most appropriate group. Most painful symptoms were classified as unrelated to PD (72.8%). Forty-seven percent of painful symptoms, however, were related to PD symptoms, such as tremor, stiffness (rigidity), toe curling, spasms, or muscle cramping. Over 25% of painful events were indirectly linked to PD as consequences of abnormal gait, poor posture, falls, near falls, fractures, or skin abrasions. A few participants (6.4%) seemed to have pain from PD treatment, such as levodopa-induced dyskinesia or lower leg edema from amantadine or a dopamine agonist. Some participants experienced restlessness or akathic movement associated with painful symptoms. Seventeen descriptors of pain could not be definitively attributed to PD, and thus were grouped in the other or multiple causes category.

Table 15

Classification of Pain in PD Axis V: M. A. Lee et al. (2006) (N = 125 for each PD pain etiology)

PD Pain Etiology	Frequency	Percent
Pain Related to Idiopathic PD	59	47.2
Pain Related to Treatment PD	8	6.4
Pain Indirectly Related to PD	32	25.6
Pain Unrelated to PD	92	73.6
Other or Multiple Causes	17	13.6

To answer question no. 1, magnitude of the relationships among the three ordinal level average pain severity categories (mild, moderate, and severe) and three clinical PD subtypes (tremor dominant, PIGD, and indeterminate PD) were examined using a 3 x 3 cross tabulation table (Table 16). Further analysis of the three PD subtypes with the three pain severity groups, using a Kruskal-Wallis Test, showed no significant relationships ($p = .256$). This finding was not surprising as 85% of participants were categorized as PIGD PD subtypes, leaving little variation for establishing meaningful relationships between average pain groups and PD subtypes.

Table 16

Crosstabulation: Average Pain Groups by Clinical PD Subtype (N = 125)

		Clinical PD Subtypes			Total
		Indeterminate	PIGD Dominant	Tremor Dominant	
Average Pain Groups	Mild	8 (6.4%)	49 (39.2%)	3 (2.4%)	60 (48.0%)
	Moderate	4 (3.2%)	39 (31.2%)	3 (2.4%)	46 (36.8%)
	Severe	0 (0.0%)	18 (14.4%)	1 (0.8%)	19 (15.2%)
Total		12 (9.6%)	106 (84.8%)	7 (5.6%)	125 (100%)

Summary of description of pain. One hundred and twenty-five participants identified 308 separate painful locations with more than half of the sample reporting three or more painful symptoms. Severity of pain was rated as moderate to severe, affecting lower limbs, lower back, and upper extremities. Pain descriptions were categorized as nociceptive or neuropathic pain, with several participants reporting both nociceptive and neuropathic pain symptoms. Most pain was characterized as nociceptive somatic pain of musculoskeletal origin.

Descriptions of temporal characteristics of pain were complex with participants ascribing more than one temporal attribute to each painful symptom. Individuals reported pain as occurring irregularly, regularly, or continuous (fluctuating and non-fluctuating). Most painful symptoms were considered unrelated to PD; however, 47.2% of painful symptoms were categorized as related to PD symptoms, and 25.6% were considered to be indirectly related to PD.

The Experience of Pain

Three multidimensional pain scales were utilized to investigate the experience of pain in PD: the Short Form - McGill Pain Questionnaire (SF-MPQ), the Brief Pain Inventory-Short Form (BPI-SF), and the Pain Catastrophizing Scale (PCS). Psychometric evaluations were performed on all of these scales as psychometric properties had not been previously reported in a PD population. Internal consistency using Cronbach's alpha was assessed for all items in the scales and subscales. Acceptable Cronbach's alphas were found for each of the scales and subscales ranging from 0.78 to 0.94 (Table 17). While desirable values for Cronbach's alphas should be 0.80 or above, measures of ≥ 0.70 are still considered acceptable (Nunnally & Bernstein, 1994).

Table 17

Pain Scale and Subscale Reliability, Cronbach's Alpha

Pain Scale	Cronbach's Alpha
Short Form - McGill Pain Questionnaire (SF-MPQ) Total	0.90
Short Form - McGill Pain Questionnaire (SF-MPQ) Sensory Subscale	0.85
Short Form - McGill Pain Questionnaire (SF-MPQ) Affective Subscale	0.81
Brief Pain Inventory Short Form (BPI-SF) Total	0.87
Brief Pain Inventory Short Form (BPI-SF), Interference Subscale	0.87
Pain Catastrophizing Scale (PCS) Total	0.94
PCS Rumination	0.89
PCS Magnification	0.78
PCS Helplessness	0.89

Table 18

Short Form - McGill Pain Questionnaire (SF-MPQ) Descriptive Data (N = 125)

	Standard				
	Mean	Deviation	Minimum	Median	Maximum
SF-MPQ Total score	16.56	10.088	1	16	45
SF-MPQ Sensory	13.10	7.373	1	13	31
SF-MPQ Affective	3.42	3.238	0	2	12

Short Form - McGill Pain Questionnaire (SF-MPQ). Two subscales of the SF-MPQ served as measures for two constructs in the Rugh (1987) Model: *perceptual-sensory system*, measured by the SF-MPQ Sensory subscale, and the *emotional-affective system*, measured by the SF-MPQ Affective subscale. Participants were asked to score 15 words on the SF-MPQ word list, from *none*, scored as 0, to *severe*, scored as 3, to indicate the absence or presence of a painful sensation for *affective* pain experience. Descriptive statistics including means, standard deviations, and minimum and maximum values, appear in Table 18. The mean score for the total

SF-MPQ score was 16.56 (± 10.09), SF-MPQ Sensory subscale 13.10 (± 7.37), and SF-MPQ Affective subscale 3.42 (± 3.24). Ironically, these scores are strikingly similar to the values reported by Melzack (1987) in women's ratings of labor pain: Sensory subscale = 13.4, Affective subscale = 3.9, and total SF-MPQ scale = 17.2. A recent study examining pain and comorbidity in older adults supports these findings with Affective subscale scores of 3.7 (± 3.1) and Sensory subscale scores of 13.2 (± 7.2) with three comorbid disease states (Leong, Farrell, Helme, & Gibson, 2007).

The SF-MPQ word list was analyzed as two subscales, Sensory (*perceptual- sensory system*) and Affective (*emotional-affective system*). The SF-MPQ Sensory subscale illustrates that most participants used "aching" to describe painful symptoms. "Stabbing" and "sharp" pain were also frequent selections representing more severe painful symptoms in the SF-MPQ Sensory subscale (Figure 2). For the SF-MPQ Affective subscale, consisting of four word choices, most participants chose "tiring" or "exhausting" to describe pain (Figure 3).

Figure 2

Sensory Subscale, Short Form - McGill Pain Questionnaire (SF-MPQ): Frequency and Rating of Word Choices

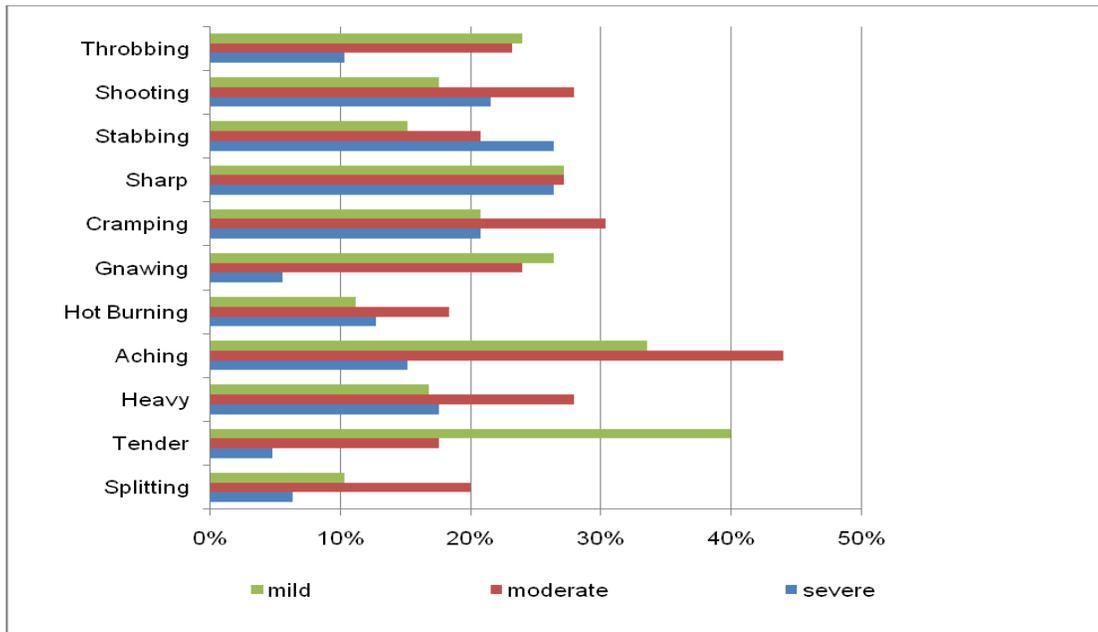
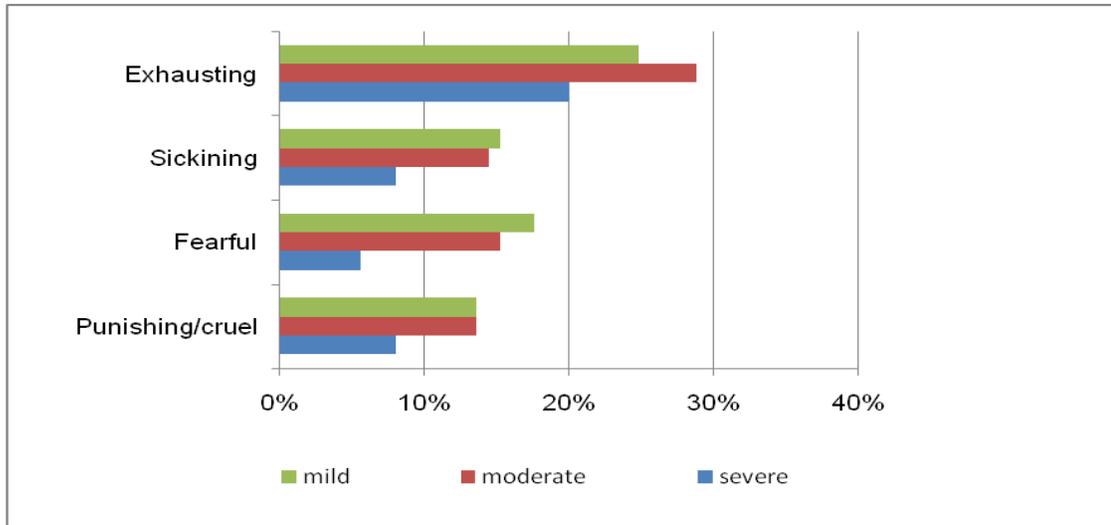


Figure 3

Affective Subscale, Short-Form - McGill Pain Questionnaire (SF-MPQ): Frequency and Rating of Word Choices



Brief Pain Questionnaire–Short Form (BPI-SF). The BPI-SF is composed of multiple item subscales, Pain Severity (corresponding to the *perceptual-sensory system*) and Pain Interference (representing the *pain behavior response system*), and one item capturing perceptions of percent of relief from current pain treatment. Inclusion criteria for the study required a score of 2 or greater, for average pain severity in the last 24 hours. Thus, the minimum average pain severity score was 2. Pain severity ratings were categorized as *no pain* = 0, *mild pain* = 1 to 4, *moderate pain* = 5 to 6, and *severe pain* = ≥ 7 and have been discussed earlier in chapter 4 (Tables 8 & 9). The Pain Interference subscale illustrates a population with mild interference in daily activities from pain, the mean Pain Interference subscale score was 3.53 (± 2.4), with the item for *difficulty with walking* approaching a moderate mean interference score of 4.1 (± 3.6). All things considered, the BPI-SF describes an overall sample with mild painful symptoms resulting in mild to moderate impairment in activities of daily life. Of the 81 participants taking pain medication, percent of pain relief was rated at 55% (± 30.6), indicating the current pain management regimen was not highly effective in providing pain relief.

Table 19

Brief Pain Inventory–Short Form (BPI-SF) Descriptive Statistics

	N	Mean	Standard Deviation	Minimum	Median	Maximum
Worst Pain	125	6.26	2.4	2	7	10
Least Pain	125	1.25	1.5	0	1	7
Average Pain	125	4.50	1.8	2	5	10
Pain Right Now	125	2.81	2.3	0	3	10
Activity Interference	125	3.94	3.2	0	3	10
Mood Interference	125	3.46	3.0	0	3	10
Walking Interference	125	4.10	3.6	0	4	10
Normal Work Interference	125	3.71	3.3	0	3	10
Interference w Relationship	125	2.45	3.0	0	1	10
Sleep Interference	125	3.05	3.3	0	2	10
Enjoyment of Life Interference	125	3.98	3.2	0	4	10
Total Interference Subscale	125	24.76	16.76	0	22	67
Mean Interference Subscale	125	3.53	2.4	0	3.14	9.57
Percent of Pain Relief	81	55.18	30.60	0	50	100

Pain Catastrophizing Scale (PCS). Catastrophizing is “an exaggerated negative mental set brought to bear during actual or anticipated painful experience” (Sullivan et al. 2004, p. 4). Catastrophizers are defined as “individuals who exaggerate the treat value or seriousness of pain sensations” (Sullivan, p. 3). The PCS was used to investigate beliefs regarding pain by measuring levels of catastrophizing. For this study, a total composite score was obtained for the PCS. There are three PCS subscales: rumination, magnification, and helplessness (Table 20). During the interview participants were asked to reflect on past painful experiences and score 13 statements on a 5-point Likert scale, scored from 0 = *Not at All* to 4 = *All the Time* (Table 20).

As a group, participants scored low on all three PCS subscales. The rumination subscale, however, demonstrated a broader range of scores with a mean of 6.72 (± 4.5). Compared to Sullivan's (2004) PCS manual, this sample of PD patients scored at the 38th percentile for the total PCS, 39th percentile for the helplessness subscale, 43rd percentile for the rumination subscale, and 46th percentile for the magnification subscale. Overall, the sample rated low levels of catastrophizing in relationship to painful symptoms. Sullivan reports a mean total PCS score of 20.9 in a sample of 851 workers being evaluated for soft tissue back injury. A score of 30 or greater represents clinically significant levels of pain catastrophizing. In this sample of PD patients, only 19 (15.2%) rated the total PCS as ≥ 30 .

Table 20

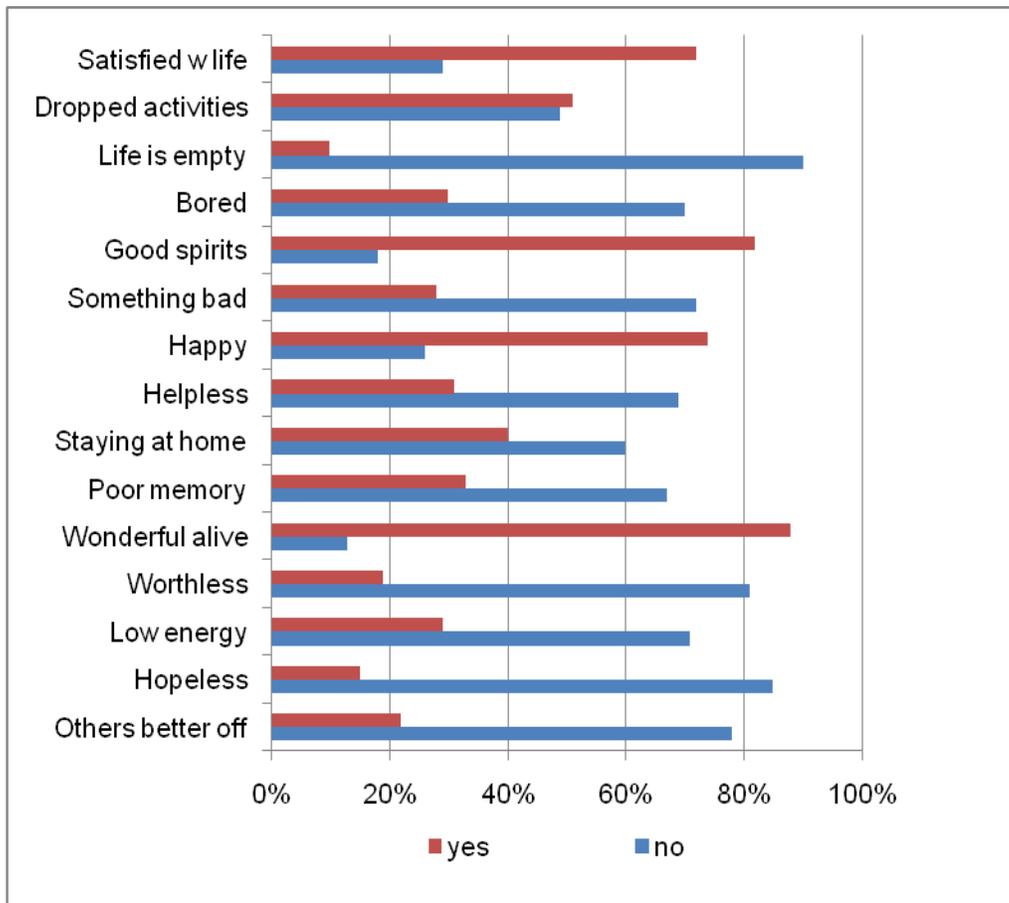
Item Descriptive Statistics for the Pain Catastrophizing Scale (PCS) (N = 125)

	Mean	Standard Deviation	Minimum	Median	Maximum
Worry all the time	0.93	1.1	0	1	4
Feel like can't go on	0.74	1.0	0	0	4
Terrible and never get better	0.89	1.1	0	0	4
Awful and overwhelms me	1.10	1.2	0	1	4
Can't stand it anymore	1.02	1.2	0	1	4
Nothing to reduce the severity	1.00	1.2	0	0	4
<u>PCS Helplessness sub scale</u>	5.68	5.5	0	3	24
Pain will get worse	0.98	1.2	0	1	4
Thinking of other painful events	0.46	0.9	0	0	4
Something serious may happen	1.00	1.3	0	1	4
<u>PCS Magnification Subscale</u>	2.45	2.8	0	1	12
Anxiously want pain to away	2.12	1.3	0	2	4
Can't seem to keep it out of mind	1.43	1.3	0	1	4
Thinking about how much it hurts	1.43	1.2	0	1	4
Want pain to stop	1.74	1.4	0	2	4
<u>PCS Rumination sub scale</u>	6.72	4.53	0	6	16
Total - PCS	14.86	11.7	0	12	48

Geriatric Depression Scale Short Form (GDS-SF). The GDS-SF served as a measure for the *emotional-affective system* within the Rugh (1987) Model, providing a measure of depressive symptoms. Consisting of 15 items, scored “yes” or “no,” the GDS-SF demonstrated that this sample of PD respondents was not experiencing significant depression. The overall mean score was 4.17 (± 3.28) with normal GDS-SF scores ranging between 0 and 4. Figure 4 graphs the percentage of participants answering “no” or “yes” to statements in the GDS-SF.

Figure 4.

Geriatric Depression Scale-Short Form (GDS-SF) Frequency of Item Responses (N=125)



Montreal Cognitive Assessment (MoCA). The MoCA was used to measure *cognitive processes* in the Rugh (1987) Model in order to gain insight into the ability of PD patients to attend to painful symptoms. Participants were tested on eight cognitive domains: attention, executive function, memory, language, visuoconstructional skills, abstract thinking, calculations,

and orientation. Table 21 shows descriptive statistics for each of the items. The sample mean was 26.29 (± 2.8), indicating that the overall score was within the range for cognitively intact individuals (normal MoCA range is ≥ 26). When scores were dichotomized above and below the criterion cut-off for being cognitively intact, 64% scored ≥ 26 , while 35.4% scored in the cognitively impaired range.

Table 21

Montreal Cognitive Assessment (MoCA): Item Descriptive Statistics (N=124)

	Mean	Standard Deviation	Minimum	Median	Maximum
Executive	3.83	0.3	0	4	5
Naming	2.81	0.42	1	3	3
Memory	1.92	0.30	0	2	2
Attention1	0.92	0.27	0	1	1
Attention2	2.76	0.60	0	3	3
Attention3	1.96	0.24	1	2	3
Language	0.83	0.38	0	1	1
Abstract	1.94	0.31	0	2	2
Delay Recall	3.25	1.34	0	3	5
Orientation	5.92	0.37	3	6	6
Total MoCA	26.29	2.80	16	27	30

Comparisons were conducted between mean pain scores for average and worst pain by the presence ($n = 59$) or absence ($n = 66$) of neuropathic-peripheral pain using independent Student's t-tests. On average, participants with neuropathic-peripheral pain reported higher mean average daily pain compared to patients without neuropathic-peripheral pain (4.95, ± 1.92 vs. 4.11, ± 1.68 , $t=2.59$, $df = 123$, $p < .01$). Likewise, participants' report of worst pain in the last 24 hours was higher for the group with neuropathic-peripheral pain compared to those without neuropathic-peripheral pain (6.92, ± 2.08 vs. 5.67, ± 2.53 , $t = 3.30$, $df = 123$, $p < .01$).

In examining the stage of disease, measured by HY scores, participants in the advanced HY PD group (n = 53) had higher levels of BPI-SF Pain Interference and pain catastrophizing compared to the moderate HY group (n = 62). Mean BPI-SF Pain Interference for the moderate group was 3.03 (± 2.41), which contrasted with the advanced HY group mean 4.12 (± 2.27) and was statistically significant ($t = -2.48$, $df = 113$, $p < .01$). The mean value for pain catastrophizing for the moderate HY group was 12.55 (± 10.97) and the mean for the advanced HY group was 18.17 (± 12.61), which was also statistically significant ($t = -2.53$, $df = 113$, $p < .01$). Similarly, patients in the advanced HY group had lower mean MoCA scores, 25.38 (± 2.98), a significant difference from the moderate HY MoCA group mean of 26.73 (± 2.5) ($t = 2.61$, $df = 112$, $p < .01$).

Variable Relationships

Comparisons Amongst Pain Severity Levels

To address the second research question, comparisons among the three BPI-SF average pain severity levels (mild 2-4, moderate 5-6, and severe 7-10) were conducted to determine if there were statistically significant differences by group for six of the participant-reported outcome measures corresponding to components of the Rugh (1987) Model. Individual one-way analysis of variance (ANOVA) tests were performed to detect overall differences, if any, followed by post-hoc analyses with Least Significant Squares (LSD) to assess where the between-group differences existed. Table 22 illustrates the results for all ANOVAs with overall F ratios, as well as p values for each. Because there were up to six different comparisons, an adjustment to alpha was made, setting it at 0.01. Statistically significant differences ($p < .01$) were found among pain groups for five of the six outcomes, with no difference by average pain severity grouping for the MoCA scores ($p = .30$). It is not clear why there was no statistically significant finding for the MoCA, except for the observation that there was little variance in the scores, overall.

Table 22

Analysis of Variance: Pain Groups (Mild, Moderate, Severe) for Six Participant Self-Reported Outcome Measures Corresponding to Components of the Rugh (1987) Model

		Sum of Squares	df	Mean Square	F	Sig.
BPI-SF Pain Interference Mean Score	Between Groups	174.561	2	87.280	19.816	<.001
	Within Groups	537.361	122	4.405		
	Total	711.922	124			
Short Form - McGill Pain Questionnaire (SF-MPQ) Sensory Subscale Score	Between Groups	939.783	2	469.891	9.881	<.001
	Within Groups	5801.865	122	47.556		
	Total	6741.648	124			
SF-MPQ Affective Subscale Score	Between Groups	108.257	2	54.129	5.539	.005
	Within Groups	1192.111	122	9.771		
	Total	1300.368	124			
Geriatric Depression Short Form (GDS-SF) Total Scale	Between Groups	107.988	2	53.994	5.367	.006
	Within Groups	1227.484	122	10.061		
	Total	1335.472	124			
Pain Catastrophizing Scale (PCS) Total Scale Score	Between Groups	1652.851	2	826.426	6.556	.002
	Within Groups	15378.557	122	126.054		
	Total	17031.408	124			
Montreal Cognitive Assessment (MoCA) Total Scale Score	Between Groups	18.822	2	9.411	1.203	.304
	Within Groups	946.726	121	7.824		
	Total	965.548	123			

Post hoc pain groups

Post hoc tests with LSD were performed with pairwise comparisons to identify statistically significant differences between the average pain intensity groups for ANOVA models that met the alpha value set at 0.01. A significant difference was found by ANOVA among the BPI-SF average pain severity groups for the BPI-SF pain interference subscale ($F(2,122) = 19.82, p < .001$), with the mean score for mild pain of 2.54 ($\pm 2.1, 95\% \text{ CI } [2.00, 3.08]$), moderate pain 3.82 ($\pm 2.1, 95\%$

CI = [3.19,4.45]), and severe pain 5.9 (± 2.1 , 95% CI = [4.94,6.97]). By post hoc analyses, participants with mild average pain reported less pain interference, compared to those with moderate (mean $d = -1.28$, 95% CI = [-2.10,-0.47], $p = .002$) and severe pain (mean $d = -3.42$, 95% CI = [-4.50, -2.32], $p < .001$). Likewise, participants with moderate average pain reported less pain interference compared to participants with severe pain (mean $d = -2.13$, 95% CI = [-3.26, -1.00], $p < .001$).

Statistically significant differences were also found by ANOVA for the SF-MPQ sensory subscale scores, and those with mild pain had a mean score of 10.32 (± 6.7), moderate pain 15.15 (± 7.3) and severe pain 16.95 (± 6.5), $F(2,122) = 9.88$, $p < .001$. Between group analyses showed participants having mild pain scored lower for sensory pain, compared to those with moderate pain (mean $d = -4.84$, 95% CI = [-7.51, -2.16], $p < .001$) and severe pain (mean $d = -6.63$, 95% CI = [-10.22, -3.04], $p < .001$). Thus, participants with higher average daily pain scores reported higher sensory pain, either by selecting more words to describe their painful symptoms or greater severity for the ones chosen.

In addition, significant findings were found among groups for affective pain (SF-MPQ, affective subscale), $F(2,122) = 5.54$, $p = .005$. Participants with mild pain had a lower mean affective pain score (2.58, ± 2.8), as compared to individuals in the severe pain group (5.21, ± 3.3), (mean $d = -2.63$, 95% CI = [-4.26, -1.00], $p = .002$). A higher score on the SF-MPQ Affective subscale is indicative that participants selected more words or rated greater severity for the affective quality of pain.

Participants differed on the degree of depression as measured by the GDS-SF, $F(2, 122) = 5.37$, $p = .006$. Significant differences were apparent between those with mild (3.60, ± 3.0) and severe (6.32, ± 3.7) pain (mean $d = -2.72$, 95% CI = [-4.37, -1.06], $p = .001$), and moderate (4.02, ± 3.1) and severe pain, (mean $d = -2.29$, 95% CI = [-4.01, -0.58], $p = .009$). By pain intensity grouping, participants with higher levels of pain had higher mean scores for depression.

Finally the post hoc analyses confirmed higher levels of catastrophizing, as measured by the PCS, in individuals with higher average daily pain levels, $F(2,122) = 6.56$, $p = .002$.

Specifically, catastrophizing scores in the mild pain group (11.53±10.2) differed significantly from the severe pain group (21.63±10.6) (mean d = -10.12, 95% CI= [-15.97, -4.26], p = .001).

Linear Regression Analysis for Predictors of Average Pain

To identify whether any of the scores obtained from the instruments used in this study were significant predictors for the BPI-SF average pain, a linear regression analysis was performed. Four variables were selected as possible predictor or explanatory variables; the subscales for the Short Form - McGill Pain Questionnaire (SF-MPQ), both Sensory and Affective subscales, and total scores from the Geriatric Depression Scale - Short Form (GDS-SF) and the Pain Catastrophizing Scale (PCS). This regression model was constructed to determine the influence, if any, of sensory and affective pain, depression and catastrophizing on reports of pain.

The results for the regression analysis appear in Table 23. While it was anticipated that higher levels of average pain would be explained by higher sensory and affective pain and levels of depression (*emotional-affective system*) and catastrophizing (*pain behavior response system*), only greater sensory pain was significant (p = .004), explaining 21.3% of the variance in average pain ($F(4,120) = 8.12, R^2 = .213, p < .01$).

Table 23

Coefficients, Dependent Variable: Average Pain Continuous Variable (BPI-SF)

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Short Form - McGill Pain Questionnaire (SF-MPQ) Sensory subscale Score	.090	.030	.360	2.973	.004
SF-MPQ Affective subscale Score	-.009	.071	-.016	-0.127	.899
Geriatric Depression Short Form (GDS-SF) Total Scale	.070	.051	.125	1.372	.173
Pain Catastrophizing Scale (PCS) Total Scale Score	.011	.018	.072	0.629	.530

Correlations

Question no. 2 examines the relationship among variables of the Rugh (1987) Model. Table 24 presents associations between the seven covariates representing the *perceptual-sensory system*, defined as pain severity and sensory quality characteristics (measured by the BPI-SF average pain severity and SF-MPQ Sensory subscale scores); the *emotional affective system*, defined as depression and affective quality characteristics (measured by the GDS-SF and SF-MPQ Affective subscale scores), *cognitive processes*, defined as beliefs and attention (measured by the MOCA and PCS), and *pain behavioral response system*, defined as pain interfering with activities of daily life (measured by the BPI-SF Pain Interference subscale).

Table 24

Associations Between Covariates, N = 125

		BPI-SF Average Pain Severity	BPI-SF Pain Interference	SF-MPQ Sensory Subscale Score	SF-MPQ Affective Subscale Score	GDS-SF Total Scale Score	PCS Total Scale Score	MoCA Total Scale Score
Brief Pain Inventory (BPI-SF) Average Pain Severity	Pearson r Sig. (2-tailed)	1	.515** <.001	.440** <.001	.329** <.001	.283** .001	.339** <.001	-.153 .089
BPI-SF Pain Interference Mean Score	Pearson r Sig. (2-tailed)	.515** <.001	1	.439** <.001	.441** <.001	.458** <.001	.532** <.001	-.201* .025
Short Form - McGill Pain Questionnaire (SF-MPQ) Sensory Subscale Score	Pearson r Sig. (2-tailed)	.440** <.001	.439** <.001	1	.709** <.001	.366** <.001	.619** <.001	-.223* .013
SF-MPQ Affective Subscale Score	Pearson r Sig. (2-tailed)	.329** <.001	.441** <.001	.709** <.001	1	.338** <.001	.644** <.001	-.220* .014
Geriatric Depression Short Form (GDS-SF) Total Scale	Pearson r Sig. (2-tailed)	.283** .001	.458** <.001	.366** <.001	.338** <.001	1	.434** <.001	-.217* .015
Pain Catastrophizing Scale (PCS) Total Scale Score	Pearson r Sig. (2-tailed)	.339** <.001	.532** <.001	.619** <.001	.644** <.001	.434** <.001	1	-.285** .001
Montreal Cognitive Assessment (MoCA) Total	Pearson r Sig. (2-tailed)	-.153 .089	-.201* .025	-.223* .013	-.220* .014	-.217* .015	-.285** .001	1

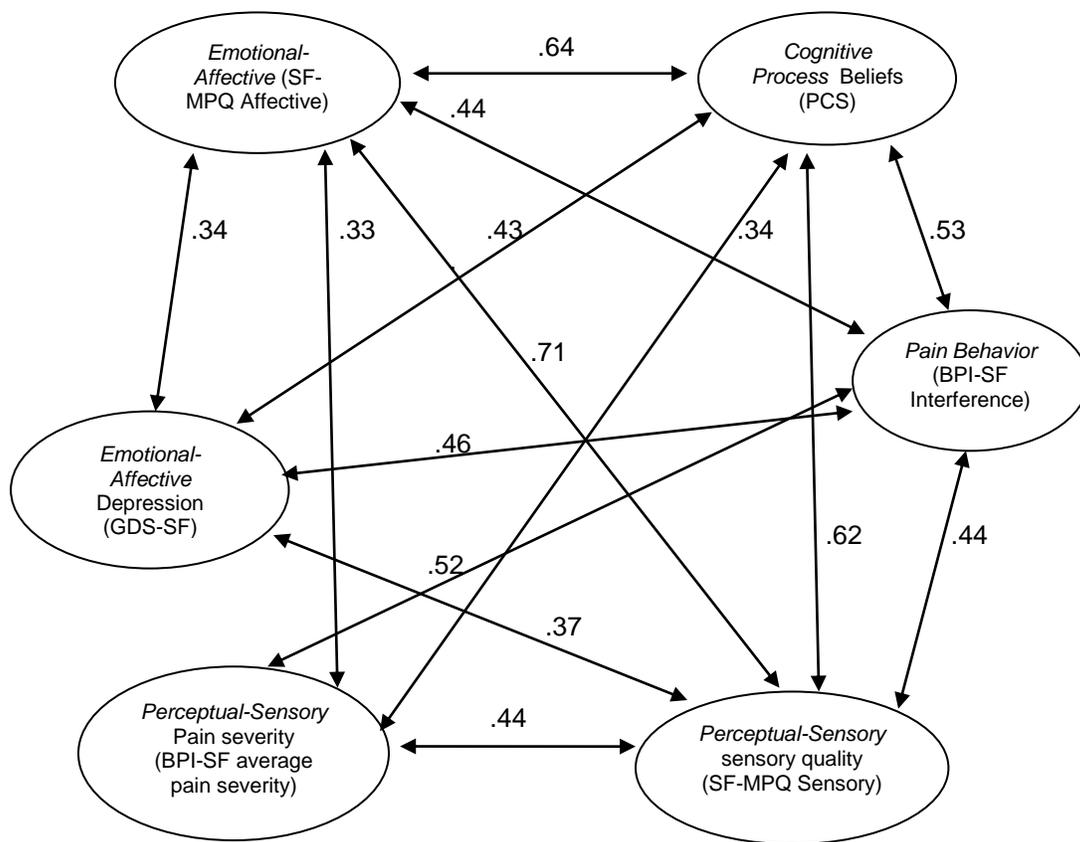
**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Figure 5 illustrates 14 significant relationships among six variables, representing components of the Rugh (1987) Model. Variables were retained in Figure 5 if their association via a Pearson's correlation (r) reached a medium to large effect size (ES), as reported in Table 24. Medium ES was accepted as $r = .30$ to $.50$ and large ES was accepted as $r > .50$ at the $\alpha = .01$ (two-tailed) level (Cohen, 1988).

Figure 5

Model of Pain in PD Correlations: Medium to Large Effect Size



Two variables measuring components of pain did not achieve statistical significance for inclusion in Figure 5. All correlations for the MoCA, used to measure cognitive processes and operationalized as the ability for an individual to attend to painful symptoms ($r = -.153$ to $-.285$), achieved significance at a small ES of .10. This finding is not surprising as the degree of variation in the MoCA scores was not substantial. The vast majority (approximately 65%) of participants scored in the normal range, with MoCA of ≥ 26 and a sample mean $26.29 (\pm 2.8)$. Correlation between BPI-SF average pain severity rating (*perceptual sensory system*) and the Geriatric Depression Scale (*emotional affective system*) ($r = .283$, two-tailed, $p < .001$) also achieved a small ES and were not included in Figure 5. The remaining 14 correlations, with medium to large effect size, were retained in the model (Figure 5) illustrating the strengths of these relationships to the experience of pain in patients with PD. The statistical significance of these relationships does not imply causality or directionality, as no directional hypothesis was posed for this inquiry.

Regression: BPI Pain Interference, Dependent variable

Lastly, question no. 2 sought to identify the influence of specific variables on Pain Interference, as captured by mean scores from seven items on the BPI-SF. Conceptually, pain interference represents an important measure of the *pain behavior response system*. Bivariate correlations were done for certain demographic variables, such as age and sex, and disease-modifying variables including length of time diagnosed with PD and stage of disease from the HY PD staging systems, thought to influence pain behavior. Since average pain and worst pain were highly correlated, $r = .707$, only average pain was selected as a possible predictor of pain interference.

Variables were examined in the model and represented in Table 25. The adjusted R^2 was .456 indicating that 46% of the variance in pain interference was explained by the model. Variables that were significantly related to pain interference, even after adjusting for age, sex, disease severity, and duration of PD were BPI-SF average pain severity (*perceptual-sensory system*) ($p < .001$), the GDS-SF scale (*emotional-affective system*) ($p = .005$), and PCS (*cognitive processes - pain beliefs*) ($p = .005$).

Table 25

Coefficients: BPI-SF Pain Interference Mean Score, Dependent Variable

Model	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
Brief Pain Inventory (BPI-SF)	.449	.103	.346	4.373	<.001
Average Pain Severity					
Short Form - McGill Pain	-.012	.035	-.036	-0.337	.737
Questionnaire (SF-MPQ) Sensory					
subscale Score					
SF-MPQ Affective subscale Score	.074	.078	.100	0.941	.349
Geriatric Depression Short Form	.160	.058	.219	2.774	.006
(GDS-SF) Total Scale					
Pain Catastrophizing Scale (PCS)	.058	.020	.283	2.824	.006
Total Scale Score					
Hoehn & Yahr Stage of Disease	-.041	.308	-.011	-0.133	.894
Sex	-.234	.371	-.045	-0.630	.530
Age	-.001	.017	-.006	-0.082	.935
PD Duration of Disease	.014	.028	.037	0.493	.623

Summary

As presented here in tables, figures, and statistics, the components of pain in PD among 125 individuals from two large urban movement disorder centers are revealed. Participants were generally well educated, older, married, Caucasian, males who were retired from active employment. Participants reported painful symptoms coincided with the onset of PD symptoms, for approximately nine years in duration. Symptoms of disease, measured by the HY stage of PD, indicated moderate to advanced disease, yet this group of patients was highly functional in measures of SE activities of daily living. A unique finding was the predominance of

the PIGD PD subtype in this sample, which has not been reported in prior PD pain literature. Participants reported at least two distinct pain locations for a total of 308 locations of pain. Most pain was categorized as nociceptive - musculoskeletal pain and 34% of the sample described both nociceptive and neuropathic pain symptoms.

Regression, correlation, and t-tests demonstrated the congruence of the Rugh (1987) Model with components of pain in PD. In an examination of pain types, those reporting neuropathic pain had higher levels of average daily pain compared to those with nociceptive pain symptoms. Participants with advanced PD reported more interference in daily activities from pain and had higher levels of negative thoughts regarding pain. Those with advanced PD also had lower MoCA scores, reflective of mild cognitive impairment. Using linear regression the SF-MPQ Sensory subscale accounted for 21% of the variance for the BPI-SF average daily pain score. Based on correlational analysis, most of the Rugh (1987) Model components of pain reached significance with medium to large effect size. The only measures to be eliminated from the model were from MoCA scores, which reached statistical significance with a small effect size.

With regard to the *pain behavioral response system*, linear regression revealed that 46% of the variance of the BPI-SF Pain Interference subscale was explained by the BPI-SF average pain severity (*perceptual-sensory system*), the GDS-SF scale (*emotional-affective system*), and the PCS (*cognitive processes - pain beliefs*). Age, sex, stage, and duration of PD symptoms did not influence the *pain behavioral response system*.

CHAPTER 5

Discussion, Limitations, Implications, and Recommendations

This chapter first addresses major findings and study limitations. Suggestions for future clinical research on the experience of pain in ambulatory patients with PD will be made. Findings will be discussed based on research questions.

Discussion of Findings

Overview

This is the first known comprehensive clinical investigation to describe and compare the experience of pain in PD using classic pain definitions driven by a theoretical model. Results provide novel insights into how variables, derived from the Rugh (1987) Model of Pain, are associated with painful symptoms in PD and mood, pain severity, pain beliefs, and interference from pain in daily life.

The first research question dealt with signs, symptoms, and manifestations associated with PD that contribute to pain based on PD subtypes and pain classifications as nociceptive, neuropathic, and mixed pain. A second research question focused on the relationships among components of pain guided by the Rugh (1987) Model: 1) *emotional-affective system*, characterized by depression and affective quality characteristics, 2) *cognitive processes* portrayed through measures of attention and pain beliefs), 3) *perceptual-sensory system* illustrated by pain severity and sensory quality characteristics of pain, and 4) a *pain behavioral response system* represented through measurement of Pain Interference.

Question no. 1: Most of the PD patients in this study were categorized as PIGD PD subtypes, with moderate to advanced disease, yet functionally independent in ADLs. Average daily pain severity rated as moderate to severe, with more than two distinct painful symptoms. Musculoskeletal pain was a common and painful symptom often reported as distressing, horrible, or excruciating. Most patients did not consider their pain as related to PD, but viewed it as commonly experienced by older adults.

Question no. 2: The Rugh (1987) Model supported higher levels of depression (*emotional-affective system*) and higher levels of average pain severity (*perceptual- sensory*

system) contributing to greater interference in daily activities (*pain behavior response*). Significant correlations exist among the *emotional-affective system*, represented by depression and affective pain quality characteristics; *cognitive processes*, measured by pain beliefs; *perceptual-sensory system* represented through measures of pain severity and pain sensory quality characteristics; and the *pain behavioral response system* evaluating interference in activities from pain in patients with PD. The Rugh Model's assumption validates that the *behavioral response system* (Pain Interference) influences the *perceptual-sensory system* (average pain severity), the *emotional-affective system* (depression), and *cognitive processes* (pain beliefs).

Characteristics of the Sample

On average, participants had been diagnosed with PD for seven years, with onset of PD symptoms and complaints of pain presenting on average two years prior to the diagnosis of disease. This supports previous reports of pain as a nonmotor PD symptom (Gilbert, 2004; O'Sullivan et al., 2008) associated with the development of rigidity and slowness of motion early in disease (Ahlskog, 2010), which describes the PIGD PD subtype. In fact, complaints of pain, stiffness, and immobility often result in referrals to a rheumatologist or an orthopedic surgeon before PD patients are seen by a neurologist (D. R. Williams & Lees, 2009). PD literature rarely discusses common painful comorbid disease states, thus, may be minimizing the unpleasant consequences of a frozen shoulder, osteoarthritis, cancer, diabetes, and back pain. Findings underscore the complexity of care that PD patients with painful comorbidity require, as well as the fact that pain in this population is underappreciated (Beiske et al., 2009; Brefel-Courbon et al., 2009; Broetz et al., 2007; M. A. Lee et al., 2006; Nebe & Ebersbach, 2009; Negre-Pages et al., 2008; Whitson et al., 2009).

Overall, participants had demographic characteristics comparable to prior studies describing pain in PD, with a slightly higher prevalence of males, probably due to recruitment at a VA movement disorder center (Broetz et al., 2007; Defazio et al., 2008; Negre-Pages et al., 2008; Roh et al., 2009). This sample was slightly younger than previous study populations, however, with a mean age of 66.83 (± 0.7) years compared to three investigations reporting mean participant age >70 years (Brefel-Courbon et al., 2009; Ebrt et al., 2009; M. A. Lee et al., 2006).

Most PD pain studies reflect the age range in this investigation, validating pain as an early nonmotor feature of disease (Ahlskog, 2010; Ford, 1998; O'Sullivan et al., 2008). In comparing PD patients to the general population, PD patients have significantly higher reports of pain on standard measures (Beiske et al., 2009).

A significant finding was the preponderance of the PIGD PD subtype in almost 85% of the study population (Jankovic et al., 1990); heretofore, this has not been reported. To establish the PIGD subtype, Jankovic et al. retrospectively examined records of 600 participants in a randomized crossover control intervention study in early PD. A cluster of symptoms (bradykinesia, postural instability, and gait difficulty) representing individuals with rapid progression of disease associated with increased functional disability was identified. Although researchers do not always use the PIGD subtype for analysis, high prevalence in this study was supported by Letro et al., (2009) who reports pain in individuals with a rigid PD clinical presentation.

In regard to other standard descriptive measures of PD, the study sample was comparable on measures of HY stage of disease, mean 2.34 (± 0.62) (Broetz et al., 2007; Letro et al., 2009; Schestatsky et al., 2007; Vela, Lyons, Singer, & Lieberman, 2007). Several studies, comparing PD patients with and without pain, report significant relationships between pain and more advanced disease (Ebrt et al., 2009; Negre-Pages et al., 2008), but others found no difference (Letro et al., 2009; Roh et al., 2009).

Researchers often cite duration of disease as a significant factor in the development of pain in PD, as advancing age is a predictor of both PD and pain (Whitson et al., 2009). PD disease duration was not significantly related to pain in several studies (Beiske et al., 2009; Broetz et al., 2007), however, as confirmed in this investigation. This may be explained by the fact that younger PD patients exhibit more pain than older PD patients (Goetz, et al., 1986).

Pain severity is reported in numerous PD studies utilizing several measures, most notably the BPI and visual analog scales. It is difficult to compare and contrast these findings with the current investigation, as this is the first study to exclude PD patients without pain. Other studies have lower BPI mean pain severity scores related to significant numbers of research

participants having no pain. For example, Beiske et al. (2009) report mean daily average pain severity as 2.85 (± 2.72) compared to a mean of 4.5 (± 1.85) here. Likewise, M.A. Lee et al. (2006) report BPI average daily pain severity as moderate in 15% and severe in 5.7%, compared to BPI average daily pain severity as moderate in 36.8% and severe in 15.2% in the current sample. Mild daily pain severity was similar between this study (48%) and that of M. A. Lee (47%).

Unique to this study is the use of the modified IASP scheme for coding chronic pain diagnoses to capture the complexity of pain. The difficulty in measuring, classifying, and reporting subjective reports of pain is evident in the identification of a mean of 2.46 (± 0.07) unique pain locations per patient, for a total of 308 pain locations in this sample. M. A. Lee et al. (2006) reported a mean of 2.3 (± 1.57) painful locations (N = 123) for a total of 285 different locations of pain, similar to the current study. Likewise, Beiske et al., (2009) reported that 30% of research participants identified multiple pain locations.

Using the IASP Pain Taxonomy Axis I criteria, primary pain regions were cervical (30%), upper shoulders or limbs (56%), lower back (67%), or lower extremities (71%). In the M. A. Lee et al. (2006) study, 285 pain locations were identified (N = 123) as: neck (9.1%), arms (10.5%), hands (6.7%), back (16.5%), feet (11.2), and legs (37.9%). Subsequent investigations by Defazio et al. (2008) and Negre-Pages et al. (2008) report similar locations of pain in community dwelling PD patients. The lack of consistent measures for pain regions limits comparisons across clinical investigations as no prior published PD pain study has utilized the IASP Axis I to report pain locations.

The modified IASP Pain Taxonomy Axis II categorized most painful symptoms as musculoskeletal (nociceptive) pain (86%) or neuropathic peripheral pain (47%), with numerous participants reporting both neuropathic and nociceptive pain (n = 43, 34.4%). In a recent report of PD patients with pain symptoms (N = 147), 53% were categorized as having more than two types of pain (Beiske et al., 2009). Of the 285 pains identified by M. A. Lee et al. (2006), 94% were categorized as nociceptive and 5.3% were reported as neuropathic syndromes. In contrast, Beiske et al. (2009) identified 70% of pain as musculoskeletal and 30% as neuropathic pain in their study of 146 PD patients with pain. Similarly, DeFazio et al. (2008) report high percentages

of neuropathic pain in PD (N = 402) and divided results into peripheral neuropathic pain (19%) and central neuropathic pain (18%).

Beiske et al. (2009) followed the Ford classification of pain in PD, which is not clearly defined. To illustrate this point, it is helpful to examine the Beiske et al. study reporting musculoskeletal pain in 70%, dystonic pain in 40%, radicular-neuropathic pain in 20%, and central neuropathic pain in 10% of PD patients. Beiske et al. defined musculoskeletal pain as related to “parkinsonian rigidity, rheumatologic disease or skeletal deformities” (p.173). This is consistent with classic pain literature defining nociceptive pain as “processing of stimuli that damages normal tissue or has the potential to do so if prolonged” (McCaffery & Pasero, 1999, p. 19). Musculoskeletal pain is a type of nociceptive pain. Nevertheless, the Beiske et al. definition of *dystonic pain* was less clear “related to antiparkinson medication” (p. 173). Dystonia is classically defined as a “syndrome of sustained muscle contractions that produce involuntary twisting and repetitive movements and abnormal postures of the trunk, neck, face, and extremities” (Tarsy, 2000). Thus, the definition of dystonia fits in the category of musculoskeletal (nociceptive) pain. Beiske et al. defines radicular-neuropathic pain as “due to a nerve root lesion, focal or peripheral neuropathy” and follows the classic pain literature on neuropathic pain (p.173). Treede et al. (2008) clarify that neuropathic pain may “arise by activity generated within the nociceptive system without adequate stimulation of its peripheral sensory endings” (p. 1630). Radicular-neuropathic pain may be equivalent to the category of neuropathic peripheral pain used in the current study. Neuropathic pain of peripheral origin is commonly seen in neurological clinical practice and is often associated with postherpetic neuralgia and diabetic neuropathy (Galer, 1995). Neuropathic central pain was defined by Beiske et al. as “disease specific symptoms in PD” (p.173). Although Beiske et al. reported 10% of pain in PD as neuropathic central pain, the current study found no clear evidence of central pain syndromes. Likewise, Defazio et al. (2008) stratified PD patients into three groups: dystonic pain (6.7%), non-dystonic pain (42.3%), and no pain (51%). Nondystonic pain was categorized as arthralgic (25.4%), cramping (11.4%), peripheral neuropathic (4.7%), and central neuropathic (4.5%) pain. These categorizations of pain are vague, but support findings that most pain experienced by individuals

with PD is musculoskeletal pain, such as osteoarthritis, fractures, and cramping pain from dystonia (Brefel-Courbon et al., 2009; Whitson et al., 2009). Pain researchers have examined the current definition of neuropathic pain to elucidate the complexity of pain categorizations (Treede et al., 2008). The identification of central neuropathic pain in the Defazio et al. study (18%) and the Beiske et al. study (10%) is of significant interest in any study of pain in PD. Both investigations will be discussed later to develop the argument that pain in PD is related to abnormal pain modulation in the CNS.

The IASP Pain Taxonomy Axis III categorized temporal characteristics of the 308 painful symptoms described by participants. This was challenging because each report of painful symptoms had temporal qualities of fluctuation and non-fluctuation, as well as regular and irregular occurrences. No known study of pain in PD has used the IASP methodology to describe temporal pain. Participants reported pain that occurred irregularly and was fluctuating in character. These descriptors of pain are consistent with prior reports in the literature, illustrating the multidimensional complexity of pain in PD (Defazio et al., 2008; Lim et al., 2008; Nebe & Ebersbach, 2009; Pacchetti et al., 1995; Silva et al., 2008).

The IASP Pain Taxonomy for pain etiology was modified for Axis V using M. A. Lee's (2006) classification of PD pain. Forty-seven percent ($n = 59$ of 125) of participants reported pain as directly related to PD symptoms such as tremor, rigidity, dystonia, or freezing of gait. Unexpectedly, the vast majority of painful symptoms were viewed as unrelated to PD (73.6%, $n = 92$ of 125). Field notes recorded pain complaints attributed to arthritis, diabetes, rotator cuff, herniated disk, spinal stenosis, sciatica, degenerative disk disease, scoliosis, spinal or cervical fusion, osteoporosis, and other common painful conditions. Participants considered pain to be indirectly related to PD in 25.6% ($n = 32$ of 125) of cases, which consisted of pain from falls, near falls, or immobility resulting in skin tears, fractures, pressure ulcers, abrasions, and bruises. Only 6.4% ($n = 8$ of 125) of painful symptoms were associated with PD treatment, such as dyskinesia, lower leg edema, and surgically implanted deep brain stimulation wires or impulse generators. In comparing these findings with those of M. A. Lee et al. (2006), pain was directly related to PD in 64.2% ($n = 79$ of 123) of cases, unrelated to PD in 62.6% ($n = 62.6\%$ of 123), indirectly related to

PD 8.1% (n = 10 of 123), and related to PD treatment in 0.8% (n = 1 of 123). Both the current and M. A. Lee et al. study are similar with regard to pain *unrelated to PD*, pain *related to PD*, and a limited number of pains *related to PD treatment*. However, there is a disparity between the number of pains *indirectly related* to PD (Lee et al. = 8.1% and current study = 25.6%), which is a result of inadequate criteria for painful symptoms *indirectly related* to PD. No other published study has utilized the Lee classification for pain; other investigations have developed unique categorization systems for recording pain in PD. For example, Negre-Pages et al. (2008) reported 40% of PD patients with persistent pain unrelated to PD, primarily osteoarthritis pain, while 60% of pain was related to PD. In describing pain, Negre-Pages et al. separated pain into two categories: “non-PD-pain” defined as “pain that was not caused or aggravated by PD” and “PD-pain” defined as “pain that was caused or aggravated by PD” (p. 1362). From these definitions, “PD-pain” divides further into “PD-pain direct and PD-pain indirect” to categorize painful symptoms in relationship to underlying comorbid painful disease states (p. 1362). The scarcity of standard descriptions of pain and its relationship to underlying disease states underscores the need for standard measures to enhance comparisons across clinical investigations.

In sum, painful symptoms are subjective and often difficult to explain. The perpetuation of inconsistent pain terms and definitions plague the PD literature, leading to difficulty comparing and contrasting clinical investigations. The use of classic pain definitions in the study of PD, as in this study, is outlined for future research dealing with the complex phenomenon of pain in PD. In this study, using an established procedure modeled after IASP research, it was possible to describe the location, category, temporal quality, and etiology of pain in PD. This methodology provides a unique opportunity to adopt a schema to formalize clinical and research investigations into pain experienced by individuals with PD.

Debating Central Pain in PD

Inconsistent definitions of pain in PD and subsequent misclassification of painful symptoms may further perpetuate the belief that a central neuropathic pain syndrome is common in PD patients. Central pain is defined as “pain initiated or caused by a primary lesion or dysfunction of the central nervous system” (Merskey & Bogduk, 1994, p. 211) and is often

associated with the complex pathophysiology of deafferentation pain, which is caused by the loss of normal sensory input resulting in abnormal pain modulation (Marbach, 1999). Examples of deafferentation pain include multiple sclerosis pain, phantom pain, or sympathetically maintained pain, such as complex regional pain syndromes (Galer, 1995). Other examples of central neuropathic pain are post stroke pain, also referred to as thalamic pain, and fibromyalgia syndrome (Andersen, Vestergaard, Ingeman-Nielsen, & Jensen, 1995; Staud, Vierck, Cannon, Mauderli, & Price, 2001). The arguments for and against a central pain syndrome in PD is mounting and is driven by assumptions formulated by the current definition of central pain (Canavero, 2009).

Following the argument of central pain as a common category of pain in PD, Schestatsky et al. (2007) investigated neurophysiologic aspects of central pain in patients with PD, hypothesizing that PD patients “have disordered integration of nociceptive inputs in brainstem centers, thalamic relay nuclei, or cortical structures” (p. 2163). Testing nine PD patients with primary central pain (PCP), nine PD patients without pain, and nine normal controls, using thermal probes and laser-evoked potentials, the team measured pain in the *on* and *off* levodopa state. Schestatsky et al. concluded that “conduction along peripheral and central pain pathways is normal in patients with PD with or without PCP” (p. 2162). Yet, the investigators did not revisit the underlying assumption that dysfunction needed to exist in central pain pathways to classify pain in PD as central pain. The current study does not investigate pain in PD as part of a central pain syndrome; however, the literature supports pain in PD as part of a complex relationship between dopamine as a central pain modulator and the pathophysiology of PD itself. The concept of PD pain as a central pain syndrome may be related to activation of descending pain pathways mediated by the basal ganglia and dopamine (Finnerup, 2008).

Dopamine, Levodopa, and Pain

The emerging literature on the role of dopamine as a neurotransmitter in the perception of pain is of great relevance to the current study. The loss of dopamine producing cells in the substantia nigra results in the classic motor symptoms of PD (tremor, rigidity, and bradykinesia) and contributes to abnormal modulation of pain centrally by activation of spinal cord neurons

through dopaminergic descending pathways (Greco et al., 2008; Mylius et al., 2009). This conceptualization of pain in PD may account for the descriptions of pain reported by PD patients as musculoskeletal pain with a fluctuating quality. Repeatedly in the literature is evidence of PD patients in the *on* levodopa state reporting less pain than PD patients in the *off* levodopa state (Gerdelat-Mas et al., 2007b; Lim et al., 2008; Nebe & Ebersbach, 2009; Schestatsky et al., 2007; Tinazzi et al., 2008; Tinazzi et al., 2009). Likewise, PD patients will complain of higher severity of pain on the more affected side, related to diminished dopamine availability to the contralateral side of the brain (Schestatsky et al.).

Although this study did not measure pain in the *on* and *off* levodopa state, nor examine levodopa dosage use, understanding the mechanism of dopamine and its relationship to pain modulation has implications for future clinical research and pain management. This complex biologic perspective is illustrated in a retrospective cohort study of dopamine agonist withdrawal syndrome in PD where patients on a dopamine agonist taper experienced anxiety, depression, agitation, irritability, and generalized pain (Rabinak & Nirenberg, 2010). This finding supports the link between dopamine and pain modulation centrally. In fact, some investigators have suggested using levodopa as an analgesic for this reason (Nebe & Ebersbach); however, long-term levodopa use is not without adverse effects and diminished efficacy (Fahn et al., 2004). Interestingly, a recent study of the effects of continuous intrajejunal levodopa infusions report improvements in nonmotor symptoms, including pain, providing an alternative to managing pain in PD (Honig et al., 2009).

Pain Models

Rugh's (1987) Model notes four pain components useful in understanding PD pain: *emotional-affective system, cognitive processes, perceptual-sensory system, and pain behavior responses* (Figure1). Rugh's Model is superior to other pain models in that there is no assumption of injury as the antecedent to pain. For example, the *Cognitive-behavioral fear-avoidance model of chronic pain* assumes injury as the first component of pain, driving catastrophizing, fear, avoidance, disability, and depression (Cook, Brawer, & Vowles, 2006). Likewise, a pain model examining depression in musculoskeletal pain assumes an *injury event* influencing pre-injury

psychopathology, stress, interference, catastrophizing, depression, coping, and social support (G.K. Lee et al., 2007). What this inquiry has established is that PD pain does not assume injury, but can be related to abnormal modulation of pain signals centrally influencing pain severity, regardless of the origin of pain. The significance of this conceptualization is the foundation for an examination of relationships among components of pain, regardless of an identifiable event. Pain is approached as a biopsychosocial process with implications for physical, psychological, social, and economic consequences (Brennan, Carr, & Cousins, 2007).

Most PD research measures pain as a single dimension of severity, limiting any understanding of pain as a multidimensional experience. Two recent investigations, however, use Health-Related Quality of Life (HrQOL) to establish an inverse relationship between depression and HrQOL in PD patients with pain (Rho et al., 2009); likewise, the DoPaMiP survey suggests persistent pain in PD is associated with diminished HrQOL and higher levels of depression and anxiety (Negre-Pages et al., 2008). The current study did not measure HrQOL and anxiety, which limits certain comparisons. Nonetheless, the study did validate higher levels of depression as significantly associated with pain severity in PD patients with pain (Ebrt et al., 2009; Goetz et al., 1987; Negre-Pages et al., 2008; Roh et al., 2009; Starkstein et al., 1991; Urakami et al., 1990).

Components of Pain in Older Adults & in Parkinson's Disease

Pain prevalence estimates for PD patients range from 40 to 85% (Beiske et al., 2009; Brefel-Courbon et al., 2009). In contrast, pain prevalence studies of community dwelling older adults estimate that 25 to 50% of elders experience persistent pain (Charette & Ferrell, 2007). One researcher concluded that pain in PD is more prevalent than in the general population, as measured by the SF-36 Bodily Pain Scale (Beiske et al.). These prevalence studies emphasize the complexity of pain and the need to understand the biology of aging and the interplay of function, depression, anxiety, cognition, pain beliefs, coping strategies, and social influences (Gibson & Farrell, 2004).

Perceptual-Sensory System. The ability to recognize the severity and quality of pain is significant in the ability of elders to communicate pain symptoms accurately. Older adults with intact verbal skills can describe symptoms in terms of severity, sensation, evaluation, and

affective quality of pain (Herr, 2005). Research comparing the perceptual sensory quality of pain in younger and older patients shows lower scores on measures of sensory quality by older adults, but similar results on pain severity. Interestingly, Goetz et al. (1986) found younger PD patients reported more pain than older PD patients. This has relevance in the neurobiology of aging, as older adults have elevated pain thresholds, implying older adults have dampening of transmission of pain in the periphery or CNS (Gibson & Farrell, 2004). This is explained by the loss of small myelinated fibers in the post mortem examinations of older animals and humans, reflecting a dysfunction in the processing of pain in the dorsal horn, which in turn affects pain modulation (Gibson & Farrell). The resulting hypoalgesia (diminished sensitivity to pain) in the elderly may thus explain the development of painful conditions without the benefit of a normal response to pain as an early warning sign. The population in this study was cognitively intact and verbally communicative in reporting pain severity and quality. A subsequent regression using age as the dependent variable did not show a difference in the *perceptual-sensory system* through measures of pain severity or pain sensory quality. This is to be expected, as only 14% of the sample was under the age of 55 years, limiting comparisons of younger and older PD patients with pain. Another possible explanation is that PD patients with pain severity (≥ 2 out of 10 points) may have self-selected, resulting in a sample without great variability in reports of pain.

The SF-MPQ Sensory subscale provides valuable information on the experience of pain, although results are limited in a cross-sectional study design. In this sample, participants chose *stabbing* and *sharp* as words that describe severe pain. *Aching* and *cramping*, however, were the most frequently chosen words to describe mild or moderate pain symptoms. Patients experiencing neuropathic pain may use *cramping* or *spasms* to describe painful symptoms (Galer, 1995). Relationships between the SF-MPQ Sensory subscale and measures of depression have been noted in other research studies (Leong et al., 2007; Sist, Florio, Miner, Lema, & Zevon, 1998; Tang, Wright, & Salkovskis, 2007). To date, no attempt to utilize the SF-MPQ to identify word patterns in PD patients with pain has been made. It has been suggested that a high correlation between the SF-MPQ Sensory and Affective subscales, as in this study, is

indicative of persistent pain states where individuals have lost the ability to differentiate the dimensions of pain (Masedo & Esteve, 2002).

Emotional-affective system. Emotional factors, such as depression and anxiety, can modify the perception of pain and are common in older adults experiencing painful symptoms (Braden et al., 2008; Rosemann, Laux, Szecsenyi, Wensing, & Grol, 2008). The directionality of depression and pain is an ongoing debate in the literature (Lopez-Lopez, Montorio, Izal, & Velasco, 2008; Mavandadi, Sorkin, Rook, & Newsom, 2007; T. E. Rudy, Weiner, Lieber, Slaboda, & Boston, 2007), yet some authors find clear indicators for depressive mood states predicting worsening of painful symptoms in older adults (Rosso, Gallagher, Luborsky, & Mossey, 2008). This study supports a relationship between low mood (*emotional-affective system*), negative pain beliefs (cognitive processes), increased interference in daily life (pain behavior), and the sensory quality of pain (*perceptual-sensory system*) in patients with PD and pain, but does not support a directional relationship in a cross-sectional design. Furthermore, the language of pain in the SF-MPQ Affective subscale identified *tiring* or *exhausting* to be the most reported descriptors for the affective quality of pain in PD. Prior reports identified *fear* and *punishment* as frequently chosen words in PD studies of pain in the *on* and *off* levodopa state (Nebe & Ebersbach, 2009).

Cognitive processes. Cognitive changes and personal beliefs form an individual's meaning of pain. Pain, as it relates to cognition, will be reviewed briefly, as the measure for cognition, MoCA scores, did not produce significant findings. Pain literature on older adults suggests cognitive impairment may distort the ability to discriminate between various unpleasant symptoms (Kelley, Siegler, & Reid, 2008). No research exists, however, to support the assumption that older adults with cognitive impairment are unable to report painful symptoms accurately, at least in the temporal report of current pain (Shega et al., 2007; Shega, Hougham, Stocking, Cox-Hayley, & Sachs, 2004). A possible explanation for the lack of significance between cognition and reports of pain, may be the increased ability of participants to attend to pain symptoms. Most of the sample had normal scores for cognition, leaving little variation in scores for analysis. Prior PD pain literature used cognitive testing for inclusion criteria, again providing no information on the experience of pain to cognitive function.

Beliefs regarding pain are operationalized based on individual judgment about painful stimuli as irrelevant, benign, or stressful (Sullivan, Rodgers et al., 2001). Literature on pain beliefs in older adults is limited, but implies elders are often reluctant to discuss pain with health care professionals, viewing it as a normal part of aging (Zanocchi et al., 2008), having a desire to be a “good” patient (Ferrell, Ferrell, & Rivera, 1995), and fear of anticipated dependence on pain medications (McAuliffe, Nay, O'Donnell, & Fetherstonhaugh, 2009). The theory of catastrophizing encompasses the concept of pain beliefs (Sullivan et al., 1995) and can serve as a measure for rumination, magnification, and helplessness associated with pain (Sullivan et al., 2005). Catastrophizing can be defined as an irrational thought that something is worse than it actually is, functioning as a significant predictor of the experience of pain (Sullivan, Thorn et al., 2001). Although there is a paucity of literature on pain catastrophizing in the elder population, it is generally assumed that catastrophic pain is significantly related to higher levels of depression and anxiety (Block & Brock, 2008). The current investigation supports these findings with catastrophic thinking (*cognitive processes* – pain beliefs) being significantly related to depression / affective quality of pain (*emotional-affective system*), interference in daily life (*pain behavior*), and pain severity / sensory quality of pain (*perceptual-sensory system*).

Pain Interference. Little empirical evidence exists for the association between components of pain and behavior in PD, specifically how pain interferes with daily life. In the geriatric pain literature, pain is examined as an early warning sign, producing changes in behavior to disrupt normal activity and promote tissue healing (Gibson & Farrell, 2004). Thus, recovery and survival are a central purpose for pain behavior (Chapman & Nakamura, 1999). Persistent pain can result in maladaptive behavior in older adults, such as decline in mobility, sleep disruption, and irritability (Pautex et al., 2006; Shega et al., 2008).

The current study utilized the BPI-SF Pain Interference subscale to represent the Rugh (1987) Model component for *pain behavior*. Prior PD research on pain used the BPI-SF scale to report the influence of pain on daily life and results support the findings of this study regarding higher pain severity related to higher reports of interference from pain in daily life (M. A. Lee et al., 2006; Negre-Pages et al., 2008). Other studies using multivariate models of pain support

significant relationships between disability and pain severity (Cook et al., 2006); pain behavior (avoidance) and depression (Lopez-Lopez et al., 2008); and interference, pain severity, and depression (G. K. Lee et al., 2007).

Limitations of the Study

The results of this study are limited by external validity with the use of a convenience sample of PD patients recruited from two large urban movement disorder centers. Participants were mostly Caucasian males with greater than high school education; therefore, results may not be generalizable to women, minorities, and individuals with lower educational levels. Participants recruited for this investigation were aware that the purpose of the study was to describe pain in PD. This may have predisposed the study to a selection bias in which PD patients with bothersome painful symptoms may have been more likely to participate, resulting in inflated estimates on study measures.

This study was a cross-sectional observational investigation, which precludes the ability to actually determine directionality in relationships observed among study variables, thus limiting internal validity. The cross-sectional design of this study precludes any capability to determine the dynamic nature of relationships between the constructs of the Rugh (1987) Model of Pain. In addition, the absence of a control group of non-PD patients with pain or PD patients without pain limits the conclusions.

Rugh (1987) (Figure 1) provides a beginning model for theoretical constructs for the study of pain in PD and drives correlations illustrated in Figure 5. Large effect size correlations were found among four constructs of the Rugh Model; however, two of these correlations may be biased, as they are subscale correlations of the same scale. The *emotional-affective system* (SF-MPQ Affective subscale) was highly correlated ($r = .71$) to the *perceptual-sensory system* (SF-MPQ Sensory subscale). The *perceptual-sensory system* (BPI-SF average pain severity) was highly correlated ($r = .52$) to the *pain behavior response system* (BPI-SF Pain Interference subscale). Caution is thus warranted when interpreting results from the multivariate model.

A final limitation is the reliance on interviews for subjective self-reports of painful symptoms and PD history, which are the foundation for conclusions generated in the

investigation. Minimal clinical data were available in medical records and no imaging studies were evaluated to confirm participants' self-reports of pain. Ideally, a study of PD and pain would include a physical exam and imaging studies to describe findings, especially in assumptions of neuropathic and nociceptive pain, as they are not mutually exclusive (Treede, et al., 2008).

Implications of Findings

For a subset of PD patients, pain is persistent and disabling. The Rugh (1987) Model, examining multiple components of pain, elucidates the complexity of pain from the biopsychosocial perspective, informing clinicians and researchers of the demanding nature of pain in PD. Pain in PD is significantly related to higher levels of depression, catastrophic thinking, and interference in activities of daily living.

This study used the classic pain definitions and the modified IASP scheme for coding chronic pain diagnosis, incorporating M. A. Lee's (2006) PD pain categories to describe pain. A need exists to reach consensus among PD researchers and pain scientists to validate these proposed classifications. The identification of PIGD PD subtypes presenting with pain is an important finding suggesting the need for assessing rigidity as a potential indication of pain in PD patients, compared to tremor predominant symptoms.

Pain is a pervasive problem for individuals living with PD and there is a paucity of literature to guide health care providers in selecting evidence-based therapy to manage pain in this unique population. This study provides evidence for the temporal fluctuations in musculoskeletal pain in PD, regardless of the identification of a causal event, lending support to the presumption of abnormal modulation of pain signals centrally. Although this study did not examine levodopa dosing among study participants, field notes confirm the report of pain fluctuation with antiparkinson medication. The low use of analgesics among study participants is validated by other research studies (Beiske et al., 2009; Ebrt et al., 2009; M. A. Lee et al., 2006) and indicates an opportunity to educate PD patients and clinicians on pain management using the World Health Organization's analgesic ladder (Wargo & Burton, 2005). Finally, pain assessment should be a priority for all PD patients to ensure adequate pharmacologic and rehabilitative therapies for managing painful symptoms.

Recommendations for Future Research

General recommendations. An overwhelming need exist for an expert review of PD pain science to establish standard pain definitions and classifications. This should include an examination of the modified IASP scheme for coding chronic pain diagnoses (Merskey & Bogduk, 1994) to establish a standard approach for reporting pain. Ideally, this endeavor would involve experts from the Movement Disorder Society and the IASP, forming a consensus panel for the study of pain in PD and publishing recommendations.

Once standard pain definitions and classifications are adopted, an emphasis on the identification of pain in PD as more than a sensory symptom becomes possible. Identification of theoretical models, such as the Rugh (1987) Model, can assist researchers in identifying variables for further investigation and comparisons with other neurodegenerative disease states. In addition, a healthy discussion of theoretical perspectives on disability and function in the PD literature would be of great benefit in the study of pain. As of now, no clearly defined or established measure for disability or function exists in the PD pain literature, leading to inconsistent use in research of these constructs. Once the groundwork is established to investigate pain in PD from the biopsychosocial perspective, with clearly defined definitions and classifications, interdisciplinary teams could incorporate measures of pain into longitudinal protocols to gain insight into how pain in PD is directionally related to other components of pain, such as depression, catastrophizing, disability, and function.

Specific recommendations. This study provides new insights into the experience of pain in older adults with PD. Despite the known link between the onset of PD symptoms and pain, little documentation of pain as a nonmotor feature early in disease has been published (Gilbert, 2004; O'Sullivan et al., 2008). This study adds evidence to a small body of literature suggesting the early onset PD and the experience of pain may be related. Pain could be a premorbid symptom of PD related to the diminishment of centrally available dopamine. Pain might also predict the development of the PIGD PD subtype. If so, timely intervention of painful symptoms could possibly even change the course of illness. Through investigation of naturalistic events, including

antiparkinson medications and standard treatments in longitudinal PD studies, these questions might eventually be answered.

The literature does not address clearly the relationship between function and disability in PD as related to pain. This study suggests that pain is often disabling, yet the sample represents a group with independent function. Perhaps individuals that are more active have more pain. As pain increases, activity may then diminish. This directionality is suggested through the relationship between average pain and the BPI-SF Pain Interference subscale. Further investigations could expand on this finding to provide insight into how individuals with PD and pain accommodate for functional limitations. Likewise, we know little of PD patients with cognitive impairment and their experience with pain. This sample was largely composed of elders with intact cognitive function and no significant findings were found among the components of pain and low MoCA scores. Research on older adults with dementia, however, demonstrates considerable untreated pain in this vulnerable population (Hadjistavropoulos et al., 2007). Capacity to recognize and report painful symptoms may have resulted in pre-selection bias; thus, future research studies should address target populations of PD patients with cognitive impairment for assessment of pain, including elicitation of caregiver perspectives of the experience of pain. Furthermore, BMI is emerging as a significant indicator of pain and has not been addressed in PD pain literature (Roberto, Perkins, & Holland, 2007). In this study, most participants were overweight. Does BMI influence the experience of pain in PD? If so, should weight reduction be considered in interventions? Likewise, do PD patients with pain become less active and thus have higher BMI?

In this study, pain in PD was mainly musculoskeletal in origin; therefore, the pain literature on musculoskeletal pain should serve as a roadmap for future protocols for PD. One such study created three profiles of patients with musculoskeletal pain to design pain interventions taking into account measures of pain severity, self-efficacy, catastrophizing, fear of injury, and disability (Denison et al., 2007). Intervention trials should include the use of nonpharmacologic therapies, such as cognitive behavioral therapy and physical therapy.

Lastly, protocols on PD and pain should strive to include women in order to address potential sex issues in pain. The general pain literature supports greater pain severity among females as compared to males (Keefe et al., 2000). This finding has been reported in recent PD literature and should be replicated for targeted pain intervention trials for women (Beiske et al., 2009; Roh et al., 2009; Vela et al., 2007).

Conclusion

This is the first known study in PD organized by classic pain definitions and structured with a theoretical model. To this end, the study contributes to both clinical research and care of patients with PD and pain. Pain, as a nonmotor symptom of PD, is often underassessed and undertreated in the clinical setting, contributing to decline in quality of life. Furthermore, it adds to the economic burden of treating individuals with this complex neurodegenerative disease. It is obvious that early identification of pain in patients with PD is crucial for the prevention of pain progression, whether from changes in neuronal plasticity or persistent neuropathic pain syndromes, to numerous other potential causes.

PD patients with pain have more negative beliefs regarding pain, low mood, and interference in activities in daily life. Furthermore, individuals with PD may experience greater pain severity compared to normal aging adults, possibly based on the neurobiology of PD and the role of dopamine in the central modulation of pain. Considering this, there should be an emphasis on optimizing antiparkinson medications to enhance dopamine levels centrally when managing PD patients with painful symptoms. Intervention trials for the treatment of pain in PD should integrate assessment for depression, as successful treatment for pain will require treatment of clinical depression in concert with effective strategies for pain management. In conclusion, clinical research on pain in PD needs to move beyond pain as a sensory symptom and examine pain from a biopsychosocial perspective.

References

- Ahlskog, J. E. (2010). Pearls: parkinsonism. *Seminars in Neurology*, 30(1), 10-14.
- American Psychiatric Association. (2000). Mood episodes. In *Diagnostic and statistical manual of mental disorders* (4 ed., pp. 320 - 232). Washington DC: Author.
- Andersen, G., Vestergaard, K., Ingeman-Nielsen, M., & Jensen, T. S. (1995). Incidence of central post-stroke pain. *Pain*, 61(2), 187-193.
- Beiske, A. G., Loge, J. H., Ronningen, A., & Svensson, E. (2009). Pain in Parkinson's disease: Prevalence and characteristics. *Pain*, 141(1-2), 173-177.
- Block, C. K., & Brock, J. (2008). The relationship of pain catastrophizing to heightened feelings of distress. *Pain Management Nursing*, 9(2), 73-80.
- Blozik, E., Stuck, A. E., Niemann, S., Ferrell, B. A., Harari, D., von Renteln-Kruse, W., et al. (2007). Geriatric Pain Measure short form: Development and initial evaluation. *Journal of the American Geriatric Society*, 55(12), 2045-2050.
- Braden, J. B., Zhang, L., Fan, M. Y., Unutzer, J., Edlund, M. J., & Sullivan, M. D. (2008). Mental health service use by older adults: the role of chronic pain. *American Journal of Geriatric Psychiatry*, 16(2), 156-167.
- Breen, J. (2002). Transitions in the concept of chronic pain. *Advances in Nursing Science*, 24(4), 48-59.
- Brefel-Courbon, C., Grolleau, S., Thalamas, C., Bourrel, R., Allaria-Lapierre, V., Loi, R., et al. (2009). Comparison of chronic analgesic drugs prevalence in Parkinson's disease, other chronic diseases and the general population. *Pain*, 141(1-2), 14-18.
- Brefel-Courbon, C., Payoux, P., Thalamas, C., Ory, F., Quelven, I., Chollet, F., et al. (2005). Effect of levodopa on pain threshold in Parkinson's disease: A clinical and positron emission tomography study. *Movement Disorders*, 20(12), 1557-1563.
- Brennan, F., Carr, D. B., & Cousins, M. (2007). Pain management: a fundamental human right. *Anesthesia and Analgesia*, 105(1), 205-221.

- Broetz, D., Eichner, M., Gasser, T., Weller, M., & Steinbach, J. P. (2007). Radicular and nonradicular back pain in Parkinson's disease: a controlled study. *Movement Disorders*, 22(6), 853-856.
- Bulpitt, C. J., Shaw, K., Clifton, P., Stern, G., Davies, J. B., & Reid, J. L. (1985). The symptoms of patients treated for Parkinson's disease. *Clinical Neuropharmacology*, 8(2), 175-183.
- Burn, D. J., Rowan, E. N., Allan, L. M., Molloy, S., O'Brien, J. T., & McKeith, I. G. (2006). Motor subtype and cognitive decline in Parkinson's disease, Parkinson's disease with dementia, and dementia with Lewy bodies. *Journal of Neurology, Neurosurgery, and Psychiatry*, 77(5), 585-589.
- Buzas, B., & Max, M. B. (2004). Pain in Parkinson disease. *Neurology*, 62(12), 2156-2157.
- Canavero, S. (2009). Central pain and Parkinson disease. *Archives of Neurology*, 66(2), 282-283; author reply 283.
- Carr, J. A. R., Honey, C. R., Sinden, M., Phillips, A. G., & Martzke, J. S. (2003). A waitlist control-group study of cognitive, mood, and quality of life outcome after posteroventral pallidotomy in Parkinson disease. *Journal of Neurosurgery*, 99(1), 78-88.
- Carroll, C. B., Bain, P. G., Teare, L., Liu, X., Joint, C., Wroath, C., et al. (2004). Cannabis for dyskinesia in Parkinson disease: A randomized double-blind crossover study. *Neurology*, 63(7), 1245-1250.
- Caviness, J. N., Driver-Dunckley, E., Connor, D. J., Sabbagh, M. N., Hentz, J. G., Noble, B., et al. (2007). Defining mild cognitive impairment in Parkinson's disease. *Movement Disorders*, 22(9), 1272-1277.
- Chapman, C. R., & Nakamura, Y. (1999). A passion of the soul: an introduction to pain for consciousness researchers. *Consciousness and Cognition*, 8(4), 391-422.
- Charette, S. L., & Ferrell, B. A. (2007). Rheumatic diseases in the elderly: assessing chronic pain. *Rheumatic Disease Clinics of North America*, 33(1), 109-122.
- Chaves, J. F., & Brown, J. M. (1987). Spontaneous cognitive strategies for the control of clinical pain and stress. *Journal of Behavioral Medicine*, 10(3), 263-276.

- Chudler, E. H., & Dong, W. K. (1995). The Role of the Basal Ganglia in Nociception and Pain. *Pain, 60*(1), 3-38.
- Cook, A. J., Brawer, P. A., & Vowles, K. E. (2006). The fear-avoidance model of chronic pain: validation and age analysis using structural equation modeling. *Pain, 121*(3), 195-206.
- Daut, R. L., Cleeland, C. S., & Flanery, R. C. (1983). Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases. *Pain, 17*(2), 197-210.
- Defazio, G., Berardelli, A., Fabbrini, G., Martino, D., Fincati, E., Fiaschi, A., et al. (2008). Pain as a nonmotor symptom of Parkinson disease: evidence from a case-control study. *Archives of Neurology, 65*(9), 1191-1194.
- Denison, E., Asenlof, P., Sandborgh, M., & Lindberg, P. (2007). Musculoskeletal pain in primary health care: Subgroups based on pain intensity, disability, self-efficacy, and fear-avoidance variables. *The Journal of Pain, 8*(1), 67-74.
- Derasari, M. D. (2003). Taxonomy of pain syndromes. In P. P. Raj (Ed.), *Pain medicine: A comprehensive review* (2nd ed.). St. Louis: Mosby.
- Dickert, N., Emanuel, E., & Grady, C. (2002). Paying research subjects: An analysis of current policies. *Annals of Internal Medicine, 136*(5), 368-373.
- Djaldetti, R., Shifrin, A., Rogowski, Z., Sprecher, E., Melamed, E., & Yarnitsky, D. (2004). Quantitative measurement of pain sensation in patients with Parkinson disease. *Neurology, 62*(12), 2171-2175.
- Ebrt, U., Larson, J. P., & Aarsland, D. (2009). Pain and its relationship to depression in parkinson disease. *American Journal of Geriatric Psychiatry, 17*(4), 269-275.
- Edwards, R. R., Smith, M. T., Kudel, I., & Haythornthwaite, J. (2006). Pain-related catastrophizing as a risk factor for suicidal ideation in chronic pain. *Pain, 126*(1-3), 272-279.
- Etchepare, F., Rozenberg, S., Mirault, T., Bonnet, A. M., Lecorre, C., Agid, Y., et al. (2006). Back problems in Parkinson's disease: An underestimated problem. *Joint Bone Spine, 73*(3), 298-302.

- Fahn, S., Elton, R. L., & Members of The UPDRS Development Committee. (1987). Unified Parkinson's disease rating scale. In S. Fahn, C. D. Marsden, M. Goldstein & D. B. Calne (Eds.), *Recent developments in Parkinson's disease* (Vol. 2, pp. 153 - 163). Florham Park, NJ: Macmillan Healthcare Information.
- Fahn, S., Oakes, D., Shoulson, I., Kieburtz, K., Rudolph, A., Lang, A., et al. (2004). Levodopa and the progression of Parkinson's disease. *New England Journal of Medicine*, 351(24), 2498-2508.
- Ferrell, B. A., Ferrell, B. R., & Rivera, L. (1995). Pain in cognitively impaired nursing home patients. *Journal of Pain and Symptom Management*, 10(8), 591-598.
- Ferrell, B. A., Stein, W. M., & Beck, J. C. (2000). The Geriatric Pain Measure: validity, reliability and factor analysis. *Journal of the American Geriatrics Society*, 48(12), 1669-1673.
- Finnerup, N. B. (2008). A review of central neuropathic pain states. *Current Opinion in Anaesthesiology*, 21(5), 586-589.
- Fisher, S. E., Burgio, L. D., Thorn, B. E., & Hardin, J. M. (2006). Obtaining self-report data from cognitively impaired elders: Methodological issues and clinical implications for nursing home pain assessment. *Gerontologist*, 46(1), 81-88.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3), 189-198.
- Ford, B. (1998). Pain in Parkinson's disease. *Clinical Neuroscience*, 5(2), 63-72.
- Ford, B., Louis, E. D., Greene, P., & Fahn, S. (1996). Oral and genital pain syndromes in Parkinson's disease. *Movement Disorders*, 11(4), 421-426.
- Ford, B., & Pfeiffer, R. (2005). Pain syndromes and disorders of sensation. In R. F. Pfeiffer & I. Bodis-Wollner (Eds.), *Parkinson's disease and nonmotor dysfunction* (pp. 255-267). Totowa, NJ: Humana Press.

- Fortner, B. V., Okon, T. A., Ashley, J., Kepler, G., Chavez, J., Tauer, K., et al. (2003). The Zero Acceptance of Pain (ZAP) Quality Improvement Project: evaluation of pain severity, pain interference, global quality of life, and pain-related costs. *Journal of Pain and Symptom Management, 25*(4), 334-343.
- Friedman, B., Heisel, M. J., & Delavan, R. L. (2005). Psychometric properties of the 15-item geriatric depression scale in functionally impaired, cognitively intact, community-dwelling elderly primary care patients. *Journal of the American Geriatrics Society, 53*(9), 1570-1576.
- Gagliese, L. (2009). Pain and aging: the emergence of a new subfield of pain research. *Journal of Pain, 10*(4), 343-353.
- Gagliese, L., & Melzack, R. (1997). Chronic pain in elderly people. *Pain, 70*(1), 3-14.
- Gagliese, L., & Melzack, R. (2003). Age-related differences in the qualities but not the intensity of chronic pain. *Pain, 104*(3), 597-608.
- Gagliese, L., & Melzack, R. (2006). Pain in the elderly. In S. B. McMahon & M. Zoltzenburg (Eds.), *Wall and Melzack's textbook of pain* (5 ed., pp. 1169-1179). London: Elsevier.
- Galer, B. S. (1995). Neuropathic pain of peripheral origin: advances in pharmacologic treatment. *Neurology, 45*(12 Suppl 9), S17-25; discussion S35-16.
- Geerlings, S. W., Twisk, J. W., Beekman, A. T., Deeg, D. J., & van Tilburg, W. (2002). Longitudinal relationship between pain and depression in older adults: sex, age and physical disability. *Social Psychiatry and Psychiatric Epidemiology, 37*(1), 23-30.
- Gerdelat-Mas, A., Simonetta-Moreau, M., Thalamas, C., Ory-Magne, F., Slaoui, T., Rascol, O., et al. (2007a). Levodopa raises objective pain threshold in Parkinson's disease: A RIII reflex study. *Journal of Neurology Neurosurgery and Psychiatry, 78*(10), 1140-1142.
- Gerdelat-Mas, A., Simonetta-Moreau, M., Thalamas, C., Ory-Magne, F., Slaoui, T., Rascol, O., et al. (2007b). Levodopa raises objective pain threshold in Parkinson's disease: a RIII reflex study. *Journal of Neurology, Neurosurgery, and Psychiatry 78*(10), 1140-1142.

- Gibson, S. J., & Farrell, M. (2004). A review of age differences in the neurophysiology of nociception and the perceptual experience of pain. *Clinical Journal of Pain, 20*(4), 227-239.
- Gilbert, G. J. (2004). Biceps pain as the presenting symptom of Parkinson disease: Effective treatment with L-dopa. *Southern Medical Journal, 97*(8), 776-777.
- Goetz, C. G., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stebbins, G. T., et al. (2007). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Process, format, and clinimetric testing plan. *Movement Disorders, 22*(1), 41-47.
- Goetz, C. G., LeWitt, P. A., & Weidenman, M. (2003). Standardized training tools for the UPDRS activities of daily living scale: newly available teaching program. *Movement Disorders, 18*(12), 1455-1458.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., et al. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders, 19*(9), 1020-1028.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Fahn, S., et al. (2003). The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Movement Disorders, 18*(7), 738-750.
- Goetz, C. G., & Stebbins, G. T. (2004). Assuring interrater reliability for the UPDRS motor section: Utility of the UPDRS teaching tape. *Movement Disorders, 19*(12), 1453-1456.
- Goetz, C. G., Tanner, C. M., Levy, M., Wilson, R. S., & Garron, D. C. (1986). Pain in Parkinson's disease. *Movement Disorders, 1*(1), 45-49.
- Goetz, C. G., Wilson, R. S., Tanner, C. M., & Garron, D. C. (1987). Relationships among pain, depression, and sleep alterations in Parkinson's disease. *Advances in Neurology, 45*, 345-347.
- Greco, R., Tassorelli, C., Armentero, M. T., Sandrini, G., Nappi, G., & Blandini, F. (2008). Role of central dopaminergic circuitry in pain processing and nitroglycerin-induced hyperalgesia. *Brain Research, 1238*, 215-223.

- Hadjistavropoulos, T., Herr, K., Turk, D. C., Fine, P. G., Dworkin, R. H., Helme, R., et al. (2007). An interdisciplinary expert consensus statement on assessment of pain in older persons. *Clinical Journal of Pain, 23*(1 Suppl), S1-43.
- Hagelberg, N., Jaaskelainen, S. K., Martikainen, I. K., Mansikka, H., Forssell, H., Scheinin, H., et al. (2004). Striatal dopamine D2 receptors in modulation of pain in humans: a review. *European Journal of Pharmacology, 500*(1-3), 187-192.
- Haythornthwaite, J. A., Clark, M. R., Pappagallo, M., & Raja, S. N. (2003). Pain coping strategies play a role in the persistence of pain in post-herpetic neuralgia. *Pain, 106*(3), 453-460.
- Herr, K. (2005). Pain assessment in the older adult with verbal communication skills. In S. J. Gibson & D. K. Weiner (Eds.), *Pain in older persons: Progress in pain research and management* (Vol. 35, pp. 111-133). Seattle: IASP Press.
- Herr, K., Coyne, P. J., Key, T., Manworren, R., McCaffery, M., Merkel, S., et al. (2006). Pain assessment in the nonverbal patient: Position statement with clinical practice recommendations. *Pain Management Nursing, 7*(2), 44-52.
- Herr, K., Spratt, K., Mobily, P. R., & Richardson, G. (2004). Pain intensity assessment in older adults - Use of experimental pain to compare psychometric properties and usability of selected pain scales with younger adults. *Clinical Journal of Pain, 20*(4), 207-219.
- Herrmann, N., Mittmann, N., Silver, I., Shulman, K. I., Busto, U., Shear, N., et al. (1996). A validation study of the geriatric depression scale short form. *International Journal of Geriatric Psychiatry, 11*, 457-460.
- Hoehn, M., & Elton, R. L. (1985). Low dosages of bromocriptine added to levodopa in Parkinson's disease. *Neurology, 35*(2), 199-206.
- Honig, H., Antonini, A., Martinez-Martin, P., Forgacs, I., Faye, G. C., Fox, T., et al. (2009). Intrajejunal levodopa infusion in Parkinson's disease: a pilot multicenter study of effects on nonmotor symptoms and quality of life. *Movement Disorders, 24*(10), 1468-1474.
- Jankovic, J., McDermott, M., Carter, J., Gauthier, S., Goetz, C., Golbe, L., et al. (1990). Variable expression of Parkinson's disease: a base-line analysis of the DATATOP cohort. The Parkinson Study Group. *Neurology, 40*(10), 1529-1534.

- Janvin, C. C., Larsen, J. P., Aarsland, D., & Hugdahl, K. (2006). Subtypes of mild cognitive impairment in Parkinson's disease: progression to dementia. *Movement Disorders, 21*(9), 1343-1349.
- Jensen, M. P., Turner, J. A., & Romano, J. M. (2007). Changes after multidisciplinary pain treatment in patient pain beliefs and coping are associated with concurrent changes in patient functioning. *Pain, 131*(1-2), 38-47.
- Karlsen, K. H., Tandberg, E., Arslan, D., & Larsen, J. P. (2000). Health related quality of life in Parkinson's disease: A prospective longitudinal study. *Journal of Neurology Neurosurgery and Psychiatry, 69*(5), 584-589.
- Karoly, P., & Ruehlman, L. S. (2007). Psychosocial aspects of pain-related life task interference: An exploratory analysis in a general population sample. *Pain Medicine, 8*(7), 563-572.
- Karp, J. F., Reynolds, C. F., Butters, M. A., Dew, M. A., Mazumdar, S., Begley, A. E., et al. (2006). The relationship between pain and mental flexibility in older adult pain clinic patients. *Pain Medicine, 7*(5), 444-452.
- Karp, J. F., Rudy, T., & Weiner, D. K. (2008). Persistent pain biases item response on the Geriatric Depression Scale (GDS): preliminary evidence for validity of the GDS-PAIN. *Pain Medicine, 9*(1), 33-43.
- Karp, J. F., Weiner, D., Seligman, K., Butters, M., Miller, M., Frank, E., et al. (2005). Body pain and treatment response in late-life depression. *American Journal of Geriatric Psychiatry, 13*(3), 188-194.
- Katz, J., & Melzack, R. (1999). Measurement of pain. *Surgical Clinics of North America, 79*(2), 231-252.
- Keefe, F. J., Lefebvre, J. C., Egert, J. R., Affleck, G., Sullivan, M. J., & Caldwell, D. S. (2000). The relationship of gender to pain, pain behavior, and disability in osteoarthritis patients: the role of catastrophizing. *Pain, 87*(3), 325-334.
- Keller, S., Bann, C. M., Dodd, S. L., Schein, J., Mendoza, T. R., & Cleeland, C. S. (2004). Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *Clinical Journal of Pain, 20*(5), 309-318.

- Kelley, A. S., Siegler, E. L., & Reid, M. C. (2008). Pitfalls and recommendations regarding the management of acute pain among hospitalized patients with dementia. *Pain Medicine*, 9(5), 581-586.
- Koller, W. C. (1984). Sensory symptoms in Parkinson's disease. *Neurology*, 34(7), 957-959.
- Kremer, E., & Atkinson, J. H., Jr. (1981). Pain measurement: construct validity of the affective dimension of the McGill Pain Questionnaire with chronic benign pain patients. *Pain*, 11(1), 93-100.
- Langston, J. W. (2006). The Parkinson's complex: parkinsonism is just the tip of the iceberg. *Annals of Neurology*, 59(4), 591-596.
- Lanoix, M. (2009). Palliative care and Parkinson's disease: managing the chronic-palliative interface. *Chronic Illness*, 5(1), 46-55.
- Lee, G. K., Chan, F., & Berven, N. L. (2007). Factors affecting depression among people with chronic musculoskeletal pain: A structural equation model. *Rehabilitation Psychology*, 52(1), 33-43.
- Lee, M. A., Prentice, W. M., Hildreth, A. J., & Walker, R. W. (2007). Measuring symptom load in Idiopathic Parkinson's disease. *Parkinsonism and Related Disorders*, 13(5), 284-289.
- Lee, M. A., Walker, R. W., Hildreth, T. J., & Prentice, W. M. (2006). A survey of pain in idiopathic Parkinson's disease. *Journal of Pain and Symptom Management*, 32(5), 462-469.
- Leeuw, M., Goossens, M. E., Linton, S. J., Crombez, G., Boersma, K., & Vlaeyen, J. W. (2007). The fear-avoidance model of musculoskeletal pain: Current state of scientific evidence. *Journal of Behavioral Medicine*, 30(1), 77-94.
- Leong, I. Y., Farrell, M. J., Helme, R. D., & Gibson, S. J. (2007). The relationship between medical comorbidity and self-rated pain, mood disturbance, and function in older people with chronic pain. *Journal of Gerontology Series A: Biological Sciences and Medical Sciences*, 62(5), 550-555.
- Letro, G. H., Quagliato, E. M., & Viana, M. A. (2009). Pain in Parkinson's disease. *Arquivos de Neuro-Psiquiatria*, 67(3A), 591-594.

- Lim, S. Y., Farrell, M. J., Gibson, S. J., Helme, R. D., Lang, A. E., & Evans, A. H. (2008). Do dyskinesia and pain share common pathophysiological mechanisms in Parkinson's disease? *Movement Disorders*, *23*(12), 1689-1695.
- Loher, T. J., Burgunder, J. M., Weber, S., Sommerhaider, R., & Krauss, J. K. (2002). Effect of chronic pallidal deep brain stimulation on off period dystonia and sensory symptoms in advanced Parkinson's disease. *Journal of Neurology Neurosurgery and Psychiatry*, *73*(4), 395-399.
- Lopez-Lopez, A., Montorio, I., Izal, M., & Velasco, L. (2008). The role of psychological variables in explaining depression in older people with chronic pain. *Aging and Mental Health*, *12*(6), 735-745.
- Marbach, J. J. (1999). Medically unexplained chronic orofacial pain. Temporomandibular pain and dysfunction syndrome, orofacial phantom pain, burning mouth syndrome, and trigeminal neuralgia. *Medical Clinics of North America*, *83*(3), 691-710.
- Marcus, D. A. (2004). Obesity and the impact of chronic pain. *Clinical Journal of Pain*, *20*(3), 186-191.
- Marsh, L., McDonald, W. M., Cummings, J., & Ravina, B. (2006). Provisional diagnostic criteria for depression in Parkinson's disease: Report of an NINDS/NIMH Work Group. *Movement Disorders*, *21*(2), 148-158.
- Martignoni, E., Franchignoni, F., Pasetti, C., Ferriero, G., & Picco, D. (2003). Psychometric properties of the Unified Parkinson's Disease Rating Scale and of the Short Parkinson's Evaluation Scale. *Journal of the Neurological Sciences*, *24*(3), 190-191.
- Martinez-Martin, P., & Forjaz, M. J. (2006). Metric attributes of the unified Parkinson's disease rating scale 3.0 battery: Part I, feasibility, scaling assumptions, reliability, and precision. *Movement Disorders*, *21*(8), 1182-1188.
- Martinez-Martin, P., Schapira, A. H., Stocchi, F., Sethi, K., Odin, P., MacPhee, G., et al. (2007). Prevalence of nonmotor symptoms in Parkinson's disease in an international setting; study using nonmotor symptoms questionnaire in 545 patients. *Movement Disorders*, *22*(11), 1623-1629.

- Masedo, A. I., & Esteve, M. R. (2002). On the affective nature of chronic pain. *Psicothema*, 14(3), 511-515.
- Massetani, R., Lucchetti, R., Vignocci, G., Siciliano, G., & Rossi, B. (1989). Pain threshold and polysynaptic components of the blink reflex in Parkinson's disease. *Functional Neurology*, 4(2), 199 - 201.
- Mavandadi, S., Sorkin, D. H., Rook, K. S., & Newsom, J. T. (2007). Pain, positive and negative social exchanges, and depressive symptomatology in later life. *Journal of Aging and Health*, 19(5), 813-830.
- McAuliffe, L., Nay, R., O'Donnell, M., & Fetherstonhaugh, D. (2009). Pain assessment in older people with dementia: literature review. *Journal of Advanced Nursing*, 65(1), 2-10.
- McCaffery, M., & Pasero, C. (1999). *Pain clinical manual* (2nd ed.). New York: Mosby.
- McDonald, D. D., & Weiskopf, C. S. (2001). Adult patients' postoperative pain descriptions and responses to the Short-Form McGill Pain Questionnaire. *Clinical Nursing Research*, 10(4), 442-452.
- Meara, J., Mitchelmore, E., & Hobson, P. (1999). Use of the GDS-15 geriatric depression scale as a screening instrument for depressive symptomatology in patients with Parkinson's disease and their carers in the community. *Age and Ageing*, 28(1), 35-38.
- Melzack, R. (1973). *The puzzle of pain*. New York: Basic Books.
- Melzack, R. (1975). The McGill Pain Questionnaire: Major properties and scoring methods. *Pain*, 1(3), 277-299.
- Melzack, R. (1983). The McGill Pain Questionnaire. In R. Melzack (Ed.), *Pain measurement and assessment* (pp. 41 - 47). New York: Raven Press.
- Melzack, R. (1987). The short-form McGill Pain Questionnaire. *Pain*, 30(2), 191-197.
- Melzack, R. (2001). Pain and the neuromatrix in the brain. *Journal of Dental Education*, 65(12), 1378-1382.
- Melzack, R., & Katz, J. (2006). Pain assessment in adult patients. In S. B. McMahon & M. Zoltzenburg (Eds.), *Wall and Melzack's textbook of pain* (5 ed., pp. 291 - 304). London: Elsevier.

- Melzack, R., & Torgerson, W. S. (1971). On the language of pain. *Anesthesiology*, 34(1), 50-59.
- Melzack, R., & Wall, P. D. (1965). Pain mechanisms: A new theory. *Science*, 150(699), 971-979.
- Melzack, R., & Wall, P. D. (1996). *The challenge of pain*. New York: Penguin Books.
- Merskey, H., & Bogduk, N. (Eds.). (1994). *Classification of chronic pain: Description of chronic pain syndromes and definitions of pain terms* (2nd ed.). Seattle: IASP Press.
- Montes-Sandoval, L. (1999). An analysis of the concept of pain. *Journal of Advanced Nursing*, 29(4), 935-941.
- Montgomery, G. K., Reynolds, N. C., Jr., & Warren, R. M. (1985). Qualitative assessment of Parkinson's disease: Study of reliability and data reduction with an abbreviated Columbia Scale. *Clinical Neuropharmacology*, 8(1), 83-92.
- Munoz, M., & Esteve, R. (2005). Reports of memory functioning by patients with chronic pain. *Clinical Journal of Pain*, 21(4), 287-291.
- Mylius, V., Engau, I., Teepker, M., Stiasny-Kolster, K., Schepelmann, K., Oertel, W. H., et al. (2009). Pain sensitivity and descending inhibition of pain in Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry*, 80(1), 24-28.
- Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., et al. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatric Society*, 53(4), 695-699.
- Nebe, A., & Ebersbach, G. (2009). Pain intensity on and off levodopa in patients with Parkinson's disease. *Movement Disorders*, 24(8), 1233-1237.
- Negre-Pages, L., Regragui, W., Bouhassira, D., Grandjean, H., & Rascol, O. (2008). Chronic pain in Parkinson's disease: the cross-sectional French DoPaMiP survey. *Movement Disorders*, 23(10), 1361-1369.
- Nunnally, J. C., & Bernstein, I. H. (1994). *Psychometric Theory*. New York: McGraw-Hill.
- O'Sullivan, S. S., Williams, D. R., Gallagher, D. A., Massey, L. A., Silveira-Moriyama, L., & Lees, A. J. (2008). Nonmotor symptoms as presenting complaints in Parkinson's disease: A clinicopathological study. *Movement Disorders*, 23(1), 101-106.

- Osborne, T. L., Jensen, M. P., Ehde, D. M., Hanley, M. A., & Kraft, G. (2007). Psychosocial factors associated with pain intensity, pain-related interference, and psychological functioning in persons with multiple sclerosis and pain. *Pain, 127*(1-2), 52-62.
- Osman, A., Barrios, F. X., Gutierrez, P. M., Kopper, B. A., Merrifield, T., & Grittmann, L. (2000). The Pain Catastrophizing Scale: Further psychometric evaluation with adult samples. *Journal of Behavioral Medicine, 23*(4), 351-365.
- Osman, A., Barrios, F. X., Kopper, B. A., Hauptmann, W., Jones, J., & O'Neill, E. (1997). Factor structure, reliability, and validity of the Pain Catastrophizing Scale. *Journal of Behavioral Medicine, 20*(6), 589-605.
- Pacchetti, C., Albani, G., Martignoni, E., Godi, L., Alfonsi, E., & Nappi, G. (1995). Off Painful Dystonia in Parkinsons-Disease Treated with Botulinum Toxin. *Movement Disorders, 10*(3), 333-336.
- Parkinson, J. (1817). *An essay on the shaking palsy*. London: Sherwood, Neely and Jones.
- Parmelee, P. (2005). Measuring mood and psychological function associated with pain in late life. In S. J. Gibson & D. K. Weiner (Eds.), *Pain in older persons: Progress in pain research and management* (Vol. 35, pp. 175 - 202). Seattle: IASP Press.
- Pasero, C. (2004). Pathophysiology of neuropathic pain. *Pain Management Nursing, 5*(4 Suppl 1), 3-8.
- Pautex, S., Michon, A., Guedira, M., Emond, H., Le Lous, P., Samaras, D., et al. (2006). Pain in severe dementia: Self-assessment or observational scales? *Journal of the American Geriatrics Society, 54*(7), 1040-1045.
- Potvin, S., Grignon, S., & Marchand, S. (2009). Human evidence of a supra-spinal modulating role of dopamine on pain perception. *Synapse, 63*(5), 390-402.
- Quinn, N. P., Koller, W. C., Lang, A. E., & Marsden, C. D. (1986). Painful Parkinson's disease. *Lancet, 1*(8494), 1366-1369.
- Quittenbam, B. H., & Grahn, B. (2004). Quality of life and pain in Parkinson's disease: a controlled cross-sectional study. *Parkinsonism & Related Disorders, 10*(3), 129-136.

- Rabinak, C. A., & Nirenberg, M. J. (2010). Dopamine agonist withdrawal syndrome in Parkinson disease. *Archives of Neurology*, *67*(1), 58-63.
- Roberto, K. A., Perkins, S. N., & Holland, A. K. (2007). Research on persistent pain in late life: current topics and challenges. *Journal of Women & Aging*, *19*(3-4), 5-19.
- Roh, J. H., Kim, B. J., Jang, J. H., Seo, W. K., Lee, S. H., Kim, J. H., et al. (2009). The relationship of pain and health-related quality of life in Korean patients with Parkinson's disease. *Acta Neurologica Scandinavica*, *119*(6), 397-403.
- Rosemann, T., Laux, G., Szecsenyi, J., Wensing, M., & Grol, R. (2008). Pain and osteoarthritis in primary care: factors associated with pain perception in a sample of 1,021 patients. *Pain Medicine*, *9*(7), 903-910.
- Rosenstiel, A. K., & Keefe, F. J. (1983). The use of coping strategies in chronic low back pain patients: Relationship to patient characteristics and current adjustment. *Pain*, *17*(1), 33-44.
- Rosso, A. L., Gallagher, R. M., Luborsky, M., & Mossey, J. M. (2008). Depression and self-rated health are proximal predictors of episodes of sustained change in pain in independently living, community dwelling elders. *Pain Medicine*, *9*(8), 1035-1049.
- Rudy, T. E., & Lieber, S. J. (2005). Functional assessment of older adults with chronic pain. In S. J. Gibson & D. K. Weiner (Eds.), *Pain in older persons: Progress in pain research and management* (Vol. 35, pp. 153 - 173). Seattle: IASP Press.
- Rudy, T. E., Weiner, D. K., Lieber, S. J., Slaboda, J., & Boston, J. R. (2007). The impact of chronic low back pain on older adults: a comparative study of patients and controls. *Pain*, *131*(3), 293-301.
- Rugh, J. D. (1987). Psychological components of pain. *Dental Clinics of North America*, *31*(4), 579-594.
- Rustoen, T., Wahl, A. K., Hanestad, B. R., Lerdal, A., Paul, S., & Miaskowski, C. (2005). Age and the experience of chronic pain: differences in health and quality of life among younger, middle-aged, and older adults. *Clinical Journal of Pain*, *21*(6), 513-523.

- Sage, J. I. (2004). Pain in Parkinson's disease. *Current Treatment Options in Neurology*, 6, 191 - 200.
- Scherder, E., Oosterman, J., Swaab, D., Herr, K., Ooms, M., Ribbe, M., et al. (2005). Recent developments in pain in dementia. *British Medical Journal* 330(7489), 461-464.
- Scherder, E., Sergeant, J. A., & Swaab, D. F. (2003). Pain processing in dementia and its relation to neuropathology. *Lancet Neurology*, 2(11), 677-686.
- Scherder, E., Wolters, E., Polman, C., Sergeant, J., & Swaab, D. (2005). Pain in Parkinson's disease and multiple sclerosis: Its relation to the medial and lateral pain systems. *Neuroscience and Biobehavioral Reviews*, 29(7), 1047-1056.
- Schestatsky, P., Kumru, H., Valls-Sole, J., Valldeoriola, F., Marti, M. J., Tolosa, E., et al. (2007). Neurophysiologic study of central pain in patients with Parkinson disease. *Neurology*, 69(23), 2162-2169.
- Schmader, K. E., & Dworkin, R. H. (2005). Clinical features and treatment of postherpetic neuralgia and peripheral neuropathy in older adults. In S. J. Gibson & D. K. Weiner (Eds.), *Pain in older adults* (pp. 355-375). Seattle: IASP Press.
- Schrag, A., Barone, P., Brown, R. G., Leentjens, A. F., McDonald, W. M., Starkstein, S., et al. (2007). Depression rating scales in Parkinson's disease: Critique and recommendations. *Movement Disorders*, 22(8), 1077-1092.
- Schuler, M., Njoo, N., Hestermann, M., Oster, P., & Hauer, K. (2004). Acute and chronic pain in geriatrics: Clinical characteristics of pain and the influence of cognition. *Pain Medicine*, 5(3), 253-262.
- Scott, B., Borgman, A., Engler, H., Johnels, B., & Aquilonius, S. M. (2000). Gender differences in Parkinson's disease symptom profile. *ACTA Neurologica Scandinavica*, 102, 37-43.
- Severeijns, R., van den Hout, M. A., Vlaeyen, J. W., & Picavet, H. S. (2002). Pain catastrophizing and general health status in a large Dutch community sample. *Pain*, 99(1-2), 367-376.
- Severeijns, R., Vlaeyen, J. W., van den Hout, M. A., & Picavet, H. S. (2004). Pain catastrophizing is associated with health indices in musculoskeletal pain: a cross-sectional study in the Dutch community. *Health Psychology*, 23(1), 49-57.

- Shega, J., Emanuel, L., Vargish, L., Levine, S. K., Bursch, H., Herr, K., et al. (2007). Pain in persons with dementia: complex, common, and challenging. *The Journal of Pain*, 8(5), 373-378.
- Shega, J., Hougham, G. W., Stocking, C. B., Cox-Hayley, D., & Sachs, G. A. (2004). Pain in community-dwelling persons with dementia: frequency, intensity, and congruence between patient and caregiver report. *Journal of Pain and Symptom Management*, 28(6), 585-592.
- Shega, J., Rudy, T., Keefe, F. J., Perri, L. C., Mengin, O. T., & Weiner, D. K. (2008). Validity of pain behaviors in persons with mild to moderate cognitive impairment. *Journal of the American Geriatrics Society*, 56(9), 1631-1637.
- Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. In T. L. Brink (Ed.), *Clinical gerontology: A guide to assessment and intervention* (pp. 165-172). New York: Haworth Press.
- Silva, E. G., Viana, M. A., & Quagliato, E. M. (2008). Pain in Parkinson's disease: analysis of 50 cases in a clinic of movement disorders. *Arquivos de Neuro-Psiquiatria*, 66(1), 26-29.
- Simmons, S. F., Ferrell, B. A., & Schnelle, J. F. (2002). Effects of a controlled exercise trial on pain in nursing home residents. *Clinical Journal of Pain*, 18(6), 380-385.
- Sist, T. C., Florio, G. A., Miner, M. F., Lema, M. J., & Zevon, M. A. (1998). The relationship between depression and pain language in cancer and chronic non-cancer pain patients. *Journal of Pain and Symptom Management*, 15(6), 350-358.
- Smith, T., Gildeh, N., & Holmes, C. (2007). The Montreal Cognitive Assessment: validity and utility in a memory clinic setting. *Canadian Journal of Psychiatry*, 52(5), 329-332.
- Snider, S. R., Fahn, S., Isgreen, W. P., & Cote, L. J. (1976). Primary sensory symptoms in parkinsonism. *Neurology*, 26(5), 423-429.
- Stacy, M., Bowron, A., Guttman, M., Hauser, R., Hughes, K., Larsen, J. P., et al. (2005). Identification of motor and nonmotor wearing-off in Parkinson's disease: Comparison of a patient questionnaire versus a clinician assessment. *Movement Disorders*, 20(6), 726-733.

- Starkstein, S. E., Preziosi, T. J., & Robinson, R. G. (1991). Sleep Disorders, Pain, and Depression in Parkinsons-Disease. *European Neurology, 31*(6), 352-355.
- Staud, R., Vierck, C. J., Cannon, R. L., Mauderli, A. P., & Price, D. D. (2001). Abnormal sensitization and temporal summation of second pain (wind-up) in patients with fibromyalgia syndrome. *Pain, 91*(1-2), 165-175.
- Strickland, D., & Bertoni, J. M. (2004). Parkinson's prevalence estimated by a state registry. *Movement Disorders, 19*(3), 318-323.
- Sullivan, M. J. L. (2004). The pain catastrophizing scale: User manual. Retrieved March 16, 2008, from <http://sullivan-painresearch.mcgill.ca/ongoing.html>
- Sullivan, M. J. L., Bishop, S. R., & Pivik, J. (1995). The Pain Catastrophizing Scale: Development and validation. *Psychological Assessment, 7*(4), 524-532.
- Sullivan, M. J. L., Lynch, M. E., & Clark, A. J. (2005). Dimensions of catastrophic thinking associated with pain experience and disability in patients with neuropathic pain conditions. *Pain, 113*(3), 310-315.
- Sullivan, M. J. L., Martel, M. O., Tripp, D., Savard, A., & Crombez, G. (2006). The relation between catastrophizing and the communication of pain experience. *Pain, 122*(3), 282-288.
- Sullivan, M. J. L., Rodgers, W. M., & Kirsch, I. (2001). Catastrophizing, depression and expectancies for pain and emotional distress. *Pain, 91*(1-2), 147-154.
- Sullivan, M. J. L., Stanish, W., Waite, H., Sullivan, M., & Tripp, D. A. (1998). Catastrophizing, pain, and disability in patients with soft-tissue injuries. *Pain, 77*(3), 253-260.
- Sullivan, M. J. L., Thorn, B., Haythornthwaite, J. A., Keefe, F., Martin, M., Bradley, L. A., et al. (2001). Theoretical perspectives on the relation between catastrophizing and pain. *Clinical Journal of Pain, 17*(1), 52-64.
- Tadros, G., & Salib, E. (2007). Elderly suicide in primary care. *International Journal of Geriatric Psychiatry, 22*(8), 750-756.
- Tan, G., Jensen, M. P., Thornby, J. I., & Shanti, B. F. (2004). Validation of the Brief Pain Inventory for chronic nonmalignant pain. *The Journal of Pain, 5*(2), 133-137.

- Tang, N. K., Wright, K. J., & Salkovskis, P. M. (2007). Prevalence and correlates of clinical insomnia co-occurring with chronic back pain. *Journal of Sleep Research, 16*(1), 85-95.
- Tarsy, D. (2000). Dystonia. In C. H. Adler & J. E. Ahlskog (Eds.), *Parkinson's Disease and Movement Disorders: Diagnosis and Treatment Guidelines for the Practicing Physician* (pp. 297-311). Totowa, NJ: Humana Press.
- Tinazzi, M., Del Vesco, C., Defazio, G., Fincati, E., Smania, N., Moretto, G., et al. (2008). Abnormal processing of the nociceptive input in Parkinson's disease: a study with CO₂ laser evoked potentials. *Pain, 136*(1-2), 117-124.
- Tinazzi, M., Del Vesco, C., Fincati, E., Ottaviani, S., Smania, N., Moretto, G., et al. (2006). Pain and motor complications in Parkinson's disease. *Journal of Neurology Neurosurgery and Psychiatry, 77*(7), 822-825.
- Tinazzi, M., Recchia, S., Simonetto, S., Defazio, G., Tamburin, S., Moretto, G., et al. (2009). Hyperalgesia and laser evoked potentials alterations in hemiparkinson: evidence for an abnormal nociceptive processing. *Journal of the Neurological Sciences, 276*(1-2), 153-158.
- Treede, R. D., Jensen, T. S., Campbell, J. N., Cruccu, G., Dostrovsky, J. O., Griffin, J. W., et al. (2008). Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology, 70*(18), 1630-1635.
- Turk, D. C., & Rudy, T. E. (1987). IASP taxonomy of chronic pain syndromes: preliminary assessment of reliability. *Pain, 30*(2), 177-189.
- Turk, D. C., Rudy, T. E., & Salovey, P. (1985). The McGill Pain Questionnaire reconsidered: confirming the factor structure and examining appropriate uses. *Pain, 21*(4), 385-397.
- Tyler, E. J., Jensen, M. P., Engel, J. M., & Schwartz, L. (2002). The reliability and validity of pain interference measures in persons with cerebral palsy. *Archives of Physical Medicine and Rehabilitation, 83*(2), 236-239.
- Ullrich, P. M., Jenson, M., Loeser, J., & Cardenas, D. (2007). Catastrophizing mediates association between pain severity, psychological distress, and functional disability among persons with spinal cord injury. *Rehabilitation Psychology, 52*(4), 390-398.

- Urakami, K., Takahashi, K., Matsushima, E., Sano, K., Nishikawa, S., & Takao, T. (1990). The threshold of pain and neurotransmitters change on pain in Parkinson's disease. *Japanese Journal of Psychiatry and Neurology*, 44(3), 589-593.
- Van Damme, S., Crombez, G., & Eccleston, C. (2004a). The anticipation of pain modulates spatial attention: Evidence for pain-specificity in high-pain catastrophizers. *Pain*, 111(3), 392-399.
- Van Damme, S., Crombez, G., & Eccleston, C. (2004b). Disengagement from pain: The role of catastrophic thinking about pain. *Pain*, 107(1-2), 70-76.
- Van Den Eeden, S. K., Tanner, C. M., Bernstein, A. L., Fross, R. D., Leimpeter, A., Bloch, D. A., et al. (2003). Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. *American Journal of Epidemiology*, 157(11), 1015-1022.
- Vaserman-Lehuede, N., & Verin, M. (1999). Shoulder pain in patients with Parkinson's disease. *Revue Du Rhumatisme*, 66(4), 220-223.
- Vela, L., Lyons, K. E., Singer, C., & Lieberman, A. N. (2007). Pain-pressure threshold in patients with Parkinson's disease with and without dyskinesia. *Parkinsonism and Related Disorders*, 13(3), 189-192.
- Wargo, B. W., & Burton, A. W. (2005). Cancer Pain. In M. S. Wallace & P. S. Staats (Eds.), *Pain medicine & management* (pp. 183 - 189). New York: McGraw-Hill.
- Weintraub, D., Oehlberg, K. A., Katz, I. R., & Stern, M. B. (2006). Test characteristics of the 15-item geriatric depression scale and Hamilton depression rating scale in Parkinson disease. *American Journal of Geriatric Psychiatry*, 14(2), 169-175.
- Weintraub, D., Saboe, K., & Stern, M. B. (2007). Effect of age on geriatric depression scale performance in Parkinson's disease. *Movement Disorders*, 22(9), 1331-1335.
- Weintraub, D., & Stern, M. B. (2005). Psychiatric complications in Parkinson disease. *American Journal of Geriatric Psychiatry*, 13(10), 844-851.
- Weintraub, D., Xie, S., Karlawish, J., & Siderowf, A. (2007). Differences in depression symptoms in patients with Alzheimer's and Parkinson's diseases: Evidence from the 15-item

- Geriatric Depression Scale (GDS-15). *International Journal of Geriatric Psychiatry*, 22(10), 1025-1030.
- Whitson, H. E., Sanders, L. L., Pieper, C. F., Morey, M. C., Oddone, E. Z., Gold, D. T., et al. (2009). Correlation between symptoms and function in older adults with comorbidity. *Journal of the American Geriatrics Society*, 57(4), 676-682.
- Wielinski, C. L., Erickson-Davis, C., Wichmann, R., Walde-Douglas, M., & Parashos, S. A. (2005). Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. *Movement Disorders*, 20(4), 410-415.
- Williams, D. R., & Lees, A. J. (2009). How do patients with parkinsonism present? A clinicopathological study. *Internal Medicine Journal*, 39(1), 7-12.
- Williams, V. S., Smith, M. Y., & Fehnel, S. E. (2006). The validity and utility of the BPI interference measures for evaluating the impact of osteoarthritic pain. *Journal of Pain and Symptom Management*, 31(1), 48-57.
- Witjas, T., Kaphan, E., Azulay, J. P., Blin, O., Ceccaldi, M., Pouget, J., et al. (2002). Nonmotor fluctuations in Parkinson's disease - Frequent and disabling. *Neurology*, 59(3), 408-413.
- Wood, P. B. (2008). Role of central dopamine in pain and analgesia. *Expert Review Neurotherapeutics*, 8(5), 781-797.
- Woolf, C. J. (2004). Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Annals of Internal Medicine*, 140(6), 441-451.
- Yesavage, J. A., Brink, T. L., Rose, T. L., Lum, O., Huang, V., Adey, M., et al. (1983). Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research*, 17(1), 37-49.
- Zadikoff, C., Fox, S. H., Tang-Wai, D. F., Thomsen, T., de Bie, R. M., Wadia, P., et al. (2008). A comparison of the mini mental state exam to the Montreal cognitive assessment in identifying cognitive deficits in Parkinson's disease. *Movement Disorders*, 23(2), 297-299.
- Zanocchi, M., Maero, B., Nicola, E., Martinelli, E., Luppino, A., Gonella, M., et al. (2008). Chronic pain in a sample of nursing home residents: prevalence, characteristics, influence on quality of life (QoL). *Archives of Gerontology and Geriatrics*, 47(1), 121-128.