A cross-sectional study investigating clinical predictors and physical experiences of pain in Parkinson's disease

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Summary

Pain is a non-motor symptom of Parkinson's disease (PD) that is often neglected due to its high prevalence in both the PD and the normal elderly population. The aims of this cross-sectional study were to establish the prevalence of pain, investigate its clinical predictors and analyze physical experiences of pain as described by PD patients.
A total of 121 patients diagnosed with PD were included. The patients underwent a neurological examination and a structured interview and completed questionnaires focusing on clinical types and physical experiences of pain. Logistic regressions were used to analyze possible predictors.
Pain was reported by 80 (66%) patients with a mean age at PD diagnosis of 67.26±11.43 years. The most common clinical types of pain experienced by the patients were dystonic pain (48%), paresthesia/neuropathic pain (36%) and musculoskeletal pain (28%). The PD patients described their physical experience of pain as aching (46%), a feeling of tension (18%), sharp pain (12%), deep pain (12%) and dull pain (11%). Patients with PD affecting the right side of the body were four times more likely to report pain on the right side of the body; however, no such relation was found for the left side of the body. A higher UPDRS-III scale score and longer PD duration reduced the likelihood of patients reporting dull pain. The presence of paresthesia/neuropathic pain was shown to decrease the likelihood of patients reporting sharp pain. No significant relationships were found between the magnitude of pain and gender, age at PD diagnosis, PD duration, UPDRS-III score, or Hoehn and Yahr stage of PD. Although 40% of the PD patients felt that medication had a (direct) effect on their pain, no relationship could be found between pain severity and PD medication.

KEY WORDS: non-motor symptoms, pain, Parkinson disease

Introduction

Parkinson's disease (PD) is a progressive neurological condition characterized by its classical motor symptoms: bradykinesia, rigidity, resting tremor and postural instability. In addition to these motor disturbances, PD also manifests itself through a variety of non-motor symptoms that include: neuropsychiatric symptoms (depression, cognitive dysfunction and dementia); sleep disorders (restless legs syndrome and insomnia); and systemic symptoms, presenting as autonomic, gastrointestinal, and sensory disturbances (Chaudhuri et al., 2006).
Pain is another common non-motor symptom of PD which can significantly affect the quality of life and normal functioning of affected individuals. In fact, pain has been a recognized clinical feature of PD since James Parkinson's earliest descriptions of the disease. Pain occurring in PD can, for diagnostic purposes and the development of intervention strategies, be classified in one or a combination of five different categories. The clinical categories of PD pain are: (i) musculoskeletal pain, (ii) radicular/neuropathic pain, (iii) dystonic pain, (iv) akathisia and, (v) central/primary parkinsonian pain (Beiske et al., 2009; Ford, 2010) (Table I, over).
The exact relationship between PD and pain is not clearly established and there has been little research in this area. Most clinical reports seem to indicate pain that is mechanical in nature at presentation and associated with the motor symptoms of the disease (Wasner and Deuschl, 2006). Musculoskeletal pain, for example, is usually attributed to the lack of mobility in PD patients due to parkinsonian rigidity (Ford, 2010). Dystonic pain is noted to be one of the most prevalent types of mechanical pain in PD patients and results from sustained twitching movements and abnormal postures (Ford, 2010). However, studies have concluded that pain in PD can have a neurological basis as well, due to altered pain pathways. Shoulder pain, commonly reported by PD patients, is thought to stem from two different mechanisms: one, directly related to the neurological symptom, is pseudorheumatic and dopamine sensitive (Letro et al., 2009); the other is thought to be associated with degenerative lesions that may worsen with the progression of PD (Letro et al., 2009). Several animal models have demonstrated varied effects, on pain

perception, of microinjection of opiates, dopamine and gamma-aminobutyric acid (GABA) in the basal ganglia, thereby confirming the existence of a neurological basis for PD pain (Chudler and Dong, 1995).

Pain is reported by as many as 40-75% of PD patients (Ford, 2010; Beiske at al., 2009; Letro et al., 2009; Defazio at al., 2008). PD is an age-related illness commonly diagnosed in the elderly and the high prevalence of pain within the general elderly population makes it difficult to establish the incidence of PD-related pain. Nevertheless, the prevalence of PD-related pain has recently become a focus of attention, as has its etiology. A recent study investigated the basic prevalence of pain (and of pain types) as a non-motor symptom in PD patients versus age-matched controls. The study found that pain was significantly more prevalent in PD patients than in the general population (Defazio et al., 2008). However, the small sample size may have contributed to the lack of any significant relationships between pain symptoms in this study. Another similar study analyzed the prevalence of pain in PD patients, its relationships with the worsening of parkinsonian symptoms, dyskinesia, depression, and the effect of levodopa on pain symptoms. No significant correlations were found between dyskinesia or depression and pain (Letro et al., 2009). A more extensive study (Beiske et al., 2009) also examined the prevalence of pain types using pain scales and inventories while also studying some of its predictors; the authors found that pain is independent of demographic and clinical variables except for female gender (Beiske et al., 2009). The types of clinical pain most commonly reported by patients in previous studies include musculoskeletal, radicular-neuropathic and dystonic pain (Hanagasi et al., 2011; Santos-Garcia et al., 2011). Depression and anxiety are common in PD patients and may also influence the perception of pain (Hanagasi et al., 2011).

A review of the literature has established that pain is a common non-motor symptom of PD and can negatively affect the quality of life of patients. However, due to its high prevalence in both the PD and the normal elderly population, this non-motor symptom remains under-reported and often neglected (Fil et al., 2013). Therefore, the aim of this cross-sectional cohort study was to analyze various clinical predictors of pain in PD that have not previously been explored. Furthermore, by focusing on how PD patients themselves report their physical experience of pain, the present study adopted an approach different from those of previous reports. This novel approach to the study of PD may provide valuable insight into new treatment options for alleviating this non-motor symptom.

Materials and methods

A total of 121 patients from a community-based Parkinson's disease clinic, diagnosed with PD, were

Table I – Five categories of pain associated with Parkinson's disease.

Category	Clinical presentation	Treatment
(i) Musculoskeletal pain	• Confined to the joints and corresponding muscles and leads to muscle tenderness, limited joint mobility and skeletal deformity. • Typical onset is with motion or after rest. • Worsened by parkinsonian rigidity, stiffness and immobility. • Described as dull, cramping or aching.	• Physical therapy. • Passive/active motion exercises. • Anti-inflammatory / analgesia medication. • Orthopedic joint surgery followed by rehabilitation.
(ii) Radicular/neuropathic pain	• Localized to specific neuronal distributions or dermatomes. • Associated with motor or sensory signs of nerve/root entrapment. • Described as tingling.	• Physical therapy and use of proper posture. • Decompressive surgery.
(iii) Dystonic pain	• Attributed to visible dystonia involving any of the extremities. Facial and pharyngeal musculature may be involved. • Onset follows sustained twisting movements and postures leading to forceful and painful muscle contractions. • Dystonia may fluctuate with varying medication dosages.	• Anticholinergics, amantadine, baclofen, apomorphine, and/or injections of botulinum toxin. • Subthalamic nucleus or globus pallidus interna stimulation.
(iv) Akathisia	• Described as a subjective feeling of restlessness.	• Levadopa, dopamine agonists, opiates.
(v) Central/primary pain	• Poorly localized pain not associated with a specific neuronal distribution or muscle groups/joints. • Described as a subjective feeling of burning/tingling pain.	• Neuropathic pain agents including: carbamazepine, gabapentin, tricyclic antidepressants, and opiates. • Levodopa and dopaminergic agents may alleviate some symptoms as well.

included in this study in 2011. In all cases, PD was diagnosed using the previously established Brain Bank Criteria (Hughes et al., 1992). These patients were routinely seen 3-4 times a year for PD-related care. Patients with a diagnosis of dementia, atypical parkinsonism or a history of trauma were excluded from the study.

Structured interviews, using a questionnaire derived from a brief pain inventory (Daut et. al., 1983), were conducted by a neurologist. Administration of the questionnaire was followed by a routine neurological examination. Questions in the interview focused predominantly on the patient's experience of physical pain (reported by patients using various physical descriptors: aching, dull, sharp, deep, and/or a feeling of tension) and on whether the pain was localized on the left or right side of the body. In order to obtain predictors for only the left or right side, patients presenting with PD on both sides of the body were excluded. Patients were also asked to report the timing of the onset of pain in relation to their initial diagnosis of PD (whether the pain appeared before, at the same time as, or after their PD diagnosis). If the patient reported the absence of pain, the interview was concluded.

During the interview, patients were asked to indicate the magnitude of their pain. Pain was initially rated using a pain scale whose values ranged in an ordinal fashion from 1 to 10 (10 being the highest rating of pain). However, due to the limited size of the sample and the small number of patients in each ordinal category, the ratings given were then merged into three broad groups: (i) low pain level (ratings 1-3), (ii) moderate pain level (ratings ratings 4-7, and (iii) high pain level (ratings 8-10).

Patients were also asked whether they felt that their PD medication had any effect on the severity of their pain. The patients who perceived a "direct" relationship between PD medication and pain reported that the medication alleviated their pain, whereas pain was exacerbated in its absence. Patients perceiving an "indirect effect" reported either an increase or a decrease in pain severity with intake of PD medication, but no change in the absence of medication. Finally, patients perceiving "no effect" felt no change in pain severity regardless of the presence or absence of PD medication.

Statistical analysis

Descriptive statistics, including demographic and clinical data, were calculated. To analyze correlations between possible predictors and pain, logistic regressions were used. The analysis of correlations between predictors included general covariates, physical descriptors and clinical types of pain, age at PD diagnosis, time since PD diagnosis, timing of pain onset in relation to initial PD diagnosis, PD stage and use of PD medication.

All statistical analyses were performed using SPSS-20. A significance value of 0.05 (p=0.05) was used.

Results

Of the 121 patients interviewed in this study, 80 (66%) reported some form of pain.

Demographical and clinical data

The mean age of the patients at PD diagnosis was 67.26±11.43 years. Pain onset occurred before PD diagnosis in 51% of the patients and after diagnosis in 47%. Demographic and clinical data are summarized in table II.

Pain characteristics

Analyzing the characteristics of pain, *aching* (46%) was found to be the most common physical predictor of pain in PD patients, followed by *tension* (18%). Dystonic pain (48%), paresthesia/neuropathic pain (36%) and musculoskeletal pain (28%) were, instead, the most common clinical types of pain. A high level of pain was reported by 37% of the patients and moderate-to-low pain by 63%. Table III (over) provides data on the pain characteristics in the eighty patients affected.

Logistic regression, analyzing pain localization in comparison to PD localization, revealed that a patient presenting with PD on the *right* side of the body is *four* times more likely to report pain on the *right* side of the body (p=0.041, Exp (B) = 4.386). By contrast, no such relations emerged between PD on the left side of the body and pain localization (either left or right, p=0.290 and p=0.293, respectively). The results are summarized in table IV (over).

Table II – Demographic and clinical data of PD patients who reported some form of pain.

Gender (n=80)	
Female	30 (38%)
Male	50 (62%)
Mean age at PD diagnosis	67.26±11.43 yrs
Mean PD duration	3.34±3.16 yrs
Timing of pain onset (n=61)	
Before PD diagnosis	31 (51%)
Same time as PD diagnosis	1 (12%)
After PD diagnosis	29 (47%)
Hoehn &Yahr Stage (n=80)	
Stage 1	0 (0%)
Stage 2	29 (36%)
Stage 3	43 (54%)
Stage 4	7 (9%)
Stage 5	1 (1%)
UPDRS-III score (n=80)	
1-10	4 (5%)
11-20	16 (32%)
21-30	37 (74%)
31-40	19 (38%)
41+	4 (5%)

Logistic regression revealed no statistically significant relationships between the magnitude of pain felt by patients and their gender or age at PD diagnosis. We also found no significant correlations between level of pain and PD duration, Unified Parkinson's Disease Rating Scale-motor section (UPDRS-III) score, or Hoehn and Yahr stage of PD. It emerged that the timing of pain onset in relation to PD diagnosis could not be used as a predictor of pain severity perceived by the patient. When keeping all other physical descriptors of pain constant, logistic regression revealed that patients reporting dull pain alone were 18 times more likely to perceive low-level pain in comparison to high-level pain (p=0.020, Exp (B)=0.055). Table V summarizes the results of the logistic regression analysis of level of pain in relation to other clinical and demographic predictors.

Table III – Pain characteristics of PD patients who reported some form of pain.

Severity of pain (n=80)	Low	15 (19%)	
	Moderate	35 (44%)	
	High	30 (37%)	
Physical experience of pain (n=80)	Aching	37 (46%)	
	Dull	11 (14%)	
	Tension	14 (18%)	
	Sharp	12 (15%)	
	Deep	12 (15%)	
Clinical type of pain (n=80)	Dystonia	38 (48%)	
	Paresthesia/neuropathic	29 (36%)	
	Akathisia	23 (29%)	
	Radicular	6 (8%)	
	Musculoskeletal	22 (28%)	
		PD on left side	*PD on right side*
Pain and PD localization (n=58)	Pain on left side	17 (25%)	12 (18%)
	Pain on right side	10 (15%)	19 (28%)

Table IV – Results of logistic regression analyzing pain localization (right vs left side of the body) in relation to PD localization (right vs left side of the body).

							OR	95%CI for Exp (B)	
		B	Std Error	Wald	df	Sig.	Exp (B)	Lower bound	Upper bound
Pain-right	Intercept	-0.124	0.827	0.022	1	0.881	--	--	--
	PD-right	1.478	0.725	4.156	1	0.041*	4.386	1.059	18.171
	PD-left	0.766	0.728	1.105	1	0.293	2.151	0.516	8.966
Pain-left	Intercept	1.997	0.930	4.611	1	0.032	--	--	--
	PD-right	-1.303	0.866	2.268	1	0.132	0.272	0.050	1.481
	PD-left	0.606	0.572	1.122	1	0.290	1.833	0.597	5.628

Table V – Results of logistic regression analyzing severity of pain in relation to other clinical and demographic predictors.

								95%CI for Exp (B)	
		B	Std Error	Wald	df	Sig.	Exp (B)	Lower Bound	Upper Bound
Low / moderate severity	Intercept	1.512	2.325	0.423	1	0.516	--	--	--
	Gender	-0.421	0.704	0.358	1	0.550	0.656	0.165	2.607
	Age diag.	-0.034	0.033	1.074	1	0.300	0.967	0.907	1.031
	Dis. dur.	-0.074	0.137	0.291	1	0.589	0.929	0.710	1.215
	UPDRS	0.502	0.409	1.509	1	0.219	1.652	0.741	3.682
	H&Y	0.261	0.610	0.183	1	0.669	1.298	0.393	4.290
High severity	Intercept	0.549	2.467	0.050	1	0.824	--	--	--
	Gender	-0.602	0.728	0.685	1	0.408	0.548	0.132	2.280
	Age diag.	-0.032	0.035	0.853	1	0.356	0.968	0.904	1.037
	Dis. dur.	0.071	0.131	0.297	1	0.586	1.074	0.831	1.388
	UPDRS	0.697	0.432	2.597	1	0.107	2.007	0.860	4.684
	H&Y	0.153	0.638	0.058	1	0.810	1.165	0.334	4.068
	Dull pain	2.908	1.251	5.407	1	0.020*	0.055	0.005	0.633

Abbreviations: Age diag.=age at PD diagnosis; Dis. dur.=duration of PD; UPDRS=score on UPDRS-III, the motor section of the Unified Parkinson's Disease Rating Scale; H&Y=Hoehn and Yahr stage of PD. *significant values (p=0.05)

Analysis of the predictors of different physical experiences of pain (pain as described by patients) revealed that every increase in the UPDRS-III scale score decreased the likelihood of patients reporting dull pain by 1.09 times (p=0.047, Exp (B)=0.917). However, this effect dissipated when other variables were kept constant (p=0.922). While keeping all other variables controlled, an increase in PD duration reduced the likelihood of patients reporting dull pain by 1.65 times (p=0.034, Exp (B)=0.607). In addition, logistic regression analysis showed that some clinical types of pain (as determined by the neurologist) can be used as predictors. The absence of paresthesia/neuropathic pain, for example, was shown to increase the likelihood of patients reporting sharp pain by 5.561 times (p=0.043, Exp (B)=5.561). On the other hand, when dystonic pain was present, the likelihood of PD patients perceiving tension pain decreased by 3.75 times (p=0.022, Exp (B)=0.267). Finally, the presence of dystonic pain or akathisia decreased the likelihood of patients describing their pain as aching (p=0.037, Exp (B)=0.272; and p=0.045, Exp (B)=0.317, respectively). No other types of pain were noted as significant predictors. Finally, when analyzing the interrelation between physical descriptors of pain, it was noted that when all other descriptors were kept constant, patients reporting aching pain were 5.529 times more likely to also report perceiving sharp pain. The results of the logistic regression analysis are given in table VI.

The effect of PD medication on pain symptoms

Patients were asked to report whether they perceived their PD medication to have any effect on the severity of their pain symptoms. 40% of the PD patients felt their medication had a direct effect, whereas 49% indicated that their medication had no effect on pain severity. Data describing the effects of PD medication on pain symptoms are summarized in table VII (over). While keeping all other variables constant, no significant relationships/predictors were noted in patients reporting a direct effect of medication. No significant changes in pain scale scores were noted with the absence or presence of medication. Furthermore, logistic regression noted no improvements in perceived pain with the use of PD medication. On analysis of the effect of wearing-off PD medication on perceived magnitude of pain, no statistically significant relationships were found. Table VIII (over) summarizes the results of the logistic regression analyzing the above-mentioned results.

Table VI – Results of logistic regression analyzing physical experiences of pain (as described by patients) and other clinical and demographic predictors.

							OR	95%CI for Exp (B)	
		B	Std Error	Wald	df	Sig.	Exp (B)	Lower bound	Upper bound
Dull pain	UPDRS	-0.087	0.044	3.937	1	0.047*	0.917	0.842	0.999
	Constant	0.102	1.051	0.009	1	0.922	1.108	--	--
	Dis. dur.	-0.499	0.236	4.486	1	0.034*	0.607	0.382	0.963
	Age diag.	-0.032	0.032	0.994	1	0.319	0.969	0.911	1.031
	H&Y	1.122	0.659	2.901	1	0.089	3.071	0.844	11.168
	UPDRS	-0.078	0.054	2.097	1	0.148	0.925	0.832	1.028
	Gender	0.457	0.763	0.358	1	0.550	1.579	0.354	7.046
	Constant	-0.182	2.112	0.007	1	0.931	0.833	--	--
	Dystonic	-0.793	0.888	0.797	1	0.372	0.452	0.079	2.581
	Pares./neuro.	0.039	0.761	0.003	1	0.959	1.040	0.234	4.616
	Akathisia	0.012	0.761	0.000	1	0.988	1.012	0.228	4.496
	Musculosk.	-0.259	1.135	0.052	1	0.819	0.772	0.083	7.138
	Constant	-1.491	1.653	0.814	1	0.367	0.225	--	--
Sharp pain	Dystonic	-0.645	0.690	0.872	1	0.350	0.525	0.136	2.031
	Pares./neuro.	1.716	0.846	4.113	1	0.043*	5.561	1.059	29.197
	Akathisia	0.587	0.698	0.709	1	0.400	1.799	0.458	7.062
	Musculosk.	0.399	1.095	0.132	1	0.716	1.490	0.174	12.742
	Constant	-2.632	0.911	8.346	1	0.004*	0.072	--	--
	Dis. dur.	-0.326	0.175	3.458	1	0.063	0.722	0.512	1.018
	Age diag.	-0.037	0.028	1.804	1	0.179	0.963	0.912	1.017
	H&Y	-0.192	0.572	0.113	1	0.737	0.825	0.269	2.532
	UPDRS	0.008	0.041	0.040	1	0.842	1.008	0.930	1.093
	Gender	-0.356	0.608	0.342	1	0.558	0.700	0.213	2.308
	Constant	2.047	1.899	1.162	1	0.281	7.743	--	--

Abbreviations: UPDRS=score on UPDRS-III, the motor section of the Unified Parkinson's Disease Rating Scale; Dis. dur.=duration of PD; Age diag.=age at PD diagnosis; H&Y=Hoehn and Yahr stage of PD; Pares./neuro.= paresthesia/neuropathic pain; Musculosk.=musculoskeletal pain; Radicular=radicular pain. *significant values (p=0.05)

Table VI (cont.) – Results of logistic regression analyzing physical experiences of pain (as described by patients) and other clinical and demographic predictors.

		B	Std Error	Wald	df	Sig.	OR Exp (B)	95%CI for Exp (B) Lower bound	Upper bound
Muscle tension pain	Dystonic	-1.319	0.576	5.250	1	0.022*	0.267	0.086	0.826
	Constant	-1.041	0.336	9.620	1	0.002*	0.353	--	--
	Dis. dur.	-0.116	0.123	0.884	1	0.347	0.891	0.700	1.134
	Age diag.	-0.026	0.026	0.994	1	0.319	0.974	0.926	1.025
	H&Y	-0.445	0.546	0.665	1	0.415	0.641	0.220	1.868
	UPDRS	-0.001	0.039	0.001	1	0.972	0.999	0.926	1.077
	Gender	0.248	0.598	0.171	1	0.679	1.281	0.397	4.139
	Constant	1.459	1.820	0.642	1	0.423	4.301	--	--
	Dystonic	-1.402	0.754	3.460	1	0.063	0.246	0.056	1.078
	Pares./neuro.	-0.933	0.647	2.080	1	0.149	0.393	0.111	1.398
	Akathisia	0.091	0.645	0.020	1	0.888	1.095	0.309	3.877
	Musculosk.	-0.130	1.112	0.014	1	0.907	0.878	0.099	7.762
	Constant	-0.430	1.443	0.089	1	0.766	0.650	--	--
Aching pain	Dystonic	-1.302	0.626	4.330	1	0.037*	0.272	0.080	0.927
	Pares./neuro.	0.389	0.551	0.497	1	0.481	1.475	0.501	4.343
	Akathisia	-1.150	0.573	4.024	1	0.045*	0.317	0.103	0.974
	Musculosk.	-1.478	0.770	3.681	1	0.055	0.228	0.050	1.032
	Radicular	-0.974	1.034	0.887	1	0.346	0.378	0.050	2.866
	Constant	2.843	1.611	3.114	1	0.078	17.17	--	--
	Dis. dur.	0.074	0.081	0.818	1	0.366	1.076	0.918	1.262
	Age diag.	0.020	0.021	0.961	1	0.327	1.021	0.980	1.063
	H&Y	0.190	0.388	0.240	1	0.624	1.209	0.566	2.586
	UPDRS	-0.035	0.031	1.256	1	0.262	0.966	0.909	1.026
	Gender	-0.243	0.431	0.319	1	0.572	0.784	0.337	1.825
	Constant	-1.451	1.452	0.999	1	0.317	0.234	--	--
	Sharp pain	1.710	0.794	4.636	1	0.031*	5.529	1.166	2.220
Deep pain	Dis. dur.	-0.191	0.163	1.370	1	0.242	0.826	0.601	1.137
	Age diag.	-0.007	0.031	0.050	1	0.823	0.993	0.934	1.056
	H&Y	0.252	0.574	0.193	1	0.660	1.287	0.418	3.961
	UPDRS	0.013	0.045	0.086	1	0.770	1.013	0.928	1.106
	Gender	-0.386	0.643	0.361	1	0.548	0.680	0.193	2.398
	Constant	-1.835	2.086	0.774	1	0.379	0.160	--	--
	Dystonic	-0.571	0.789	0.524	1	0.469	0.565	0.120	2.652
	Pares./neuro.	-0.949	0.800	1.408	1	0.235	0.387	0.081	1.857
	Akathisia	0.902	0.749	1.449	1	0.229	2.463	0.568	10.689
	Musculosk.	-0.644	1.058	0.371	1	0.542	0.525	0.066	4.175
	Constant	-1.589	0.866	3.366	1	0.067	0.204	--	--

Abbreviations: UPDRS=score on UPDRS-III, the motor section of the Unified Parkinson's Disease Rating Scale; Dis. dur.=duration of PD; Age diag.=age at PD diagnosis; H&Y=Hoehn and Yahr stage of PD; Pares./neuro.= paresthesia/neuropathic pain; Musculosk.=musculoskeletal pain; Radicular=radicular pain. *significant values (p=0.05)

Table VII – Patients' perceptions of the effects of PD medication on pain symptoms

Effect	Low pain severity	Moderate pain severity	High pain severity	Total (n=45)
Direct	1 (2.22%)	8 (17.78%)	9 (20%)	18 (40%)
Indirect	1 (2.22%)	2 (4.44%)	2 (4.44%)	5 (11.11%)
No effect	3 (6.67%)	13 (28.89%)	6 (13.33%)	22 (48.89%)

Table VIII – Results of logistic regression between the severity of pain and use of PD medication.

	B	Std Error	Wald	df	Sig.	Exp (B)	95%CI for Exp (B) Lower Bound	Upper Bound
Low/moderate severity								
Direct effect	0.758	1.201	0.398	1	0.528	2.133	0.203	22.444
Improvement with PD medication	0.542	0.924	0.344	1	0.558	1.719	0.281	10.509
PD medication wearing off	-0.028	0.948	0.001	1	0.976	0.972	0.152	6.231
High severity								
Direct effect	1.504	1.219	1.522	1	0.217	4.500	0.413	49.077
Improvement with PD medication	1.179	0.936	1.584	1	0.208	3.250	0.519	20.370
PD medication wearing off	1.368	0.966	2.005	1	0.157	3.929	0.591	26.107

Discussion

In this sample, 80 of the 121 (66%) PD patients reported some form of pain. It should be noted, however, that PD is a disease that predominantly affects the elderly population. In our study, the mean age at the time of PD diagnosis was 67.26±11.43 years. Pain within the general population also tends to increase with age. As reported in a previous study, measuring pain prevalence rates in the PD population without age-matched controls can lead to an overestimation of the true prevalence of pain (Beiske et al., 2009). This observation may be further supported by the fact that in our study, an equal number of patients reported the onset of pain before (50.82%) and after (47.54%) their diagnosis of PD. However, the onset of PD may occur well before its diagnosis by a neurologist. Although the present study lacked a control group, a review of the previous literature has clearly established a significantly higher incidence of pain within the PD population in comparison to the general population (Beiske et al., 2009; Letro et al., 2009). Furthermore, the prevalence of pain reported in the present study is comparable to previously reported prevalence rates (Hanagasi et al, 2011; Ford, 2010; Beiske et al., 2009; Letro et al., 2009). Additionally, due to our strict inclusion and exclusion criteria (patients with dementia were excluded), it is assumed that the patients' accounts were valid and therefore that the prevalence rate reported is representative of pain experienced within the PD population. Dystonic pain, parathesia/neuropathic pain and musculoskeletal pain were the most prevalent types of clinical pain experienced by our patients, and these findings are consistent with those of previous studies.

As expected, PD localized on the right side of the body increased the likelihood of the patient reporting pain on the right side of the body. Interestingly, the opposite did not hold true. PD localized on the left side could not be used as a significant predictor of pain on either the left or the right side of the body. This may be explained by the dominance of one half of the body over the other: within the general population (including PD patients), most individuals have a dominant right side. Therefore, the pain symptoms of patients presenting with PD localized on the right side of the body may be significantly exacerbated by their more frequent use or motion of that side. By contrast, PD localized on the left side of the body was not found to be correlated with patient reports of pain on the left side, a result that may be due to the infrequent use of this side of the body by the "right-handed" majority. It should also be noted that pain can be non-localized in nature as observed in akathisia or primary/secondary parkinsonian pain (Ford, 2010). Hence, some patients reporting pain may have been unable to localize it to a specific side of their body.

Like previous authors (Beiske et al., 2009; Lee et al., 2006), we found no significant correlations between magnitude of pain and PD duration, UPDRS-III score or Hoehn and Yahr stage of PD, even though one might imagine that increasing severity of PD symptoms would be paralleled by increasing pain symptoms, including pain associated with both the mechanical and neurological aspects of the disease. Our study confirms the findings of the previous investigations and indicates that the magnitude of pain may be independent of demographic and clinical variables. This, however, suggests that the use of longitudinal studies of PD patients experiencing pain is warranted in order to examine how pain perception may change over the course of the disease. Another explanation of this finding may be found within the demographic data of the patient sample used in this study. Perception and reporting of pain were found to be highly variable between individuals and may be dependent on a variety of factors including age, gender, and even ethnicity. The sample in the present study was derived from a community-based Parkinson's disease clinic, and a majority of the patients analyzed were immigrants from different backgrounds. This may be linked to the variability in the reporting that could not be reasonably controlled within the study.

Dull pain was seen to be associated with patient reports of low pain severity, as might be expected. This finding is further supported by the fact that increases in UPDRS-III scale scores and PD duration each reduced the likelihood of patients reporting dull pain. Hence, it is possible that rather than these variables having an effect on the magnitude of pain, as

initially predicted, the patient's pain evolves leading him to experience different types of pain. Changes in the type of pain experienced may result in pain severity changes that are too small to be detected in a study with a limited sample size. Longitudinal studies using larger sample sizes or systematic reviews using data from this and other similar studies may be warranted to explore the relationship between these variables as the disease progresses.

The present study also confirms some of the clinical types of pain and their associated physical descriptors. The presence of paresthesia/neuropathic pain, for example, was shown to decrease the likelihood of patients reporting sharp pain. It has been reported that this pain category is usually associated with a feeling of tingling that is congruent with neuronal distributions and dermatomes (Ford, 2010). Dystonic pain, on the other hand, consists of powerful muscle spasms capable of masking lower intensity pain, like tension or aching. Akathisia (a feeling of restlessness) is generally not associated with aching pain, as confirmed in the present study.

In many cases, patients can experience more than one type of pain depending upon the etiology. Back pain has been reported to be present in up to 74% of PD patients, which may or may not be attributable to PD and can belong to more than one type of pain category (Ha and Jankovic, 2012). In our sample, 28% of the PD patients experienced more than one type of pain and 8% used more than one type of physical descriptor to describe their pain.

Most of the patients in the present study stated that their PD medication had a direct or no effect on their pain symptoms. Most patients reporting a direct effect rated their pain severity as moderate or high on the pain scale. These patients, presumably due to the magnitude of their pain experienced most relief, hence the high amount of subjects in these two categories. By contrast, patients suffering from low pain may not have been able to notice minor changes in their pain scale when taking PD medication and to report these on their pain scale. The patients reporting no effect of their PD medication on their pain symptoms mostly gave moderate-to-high pain scale ratings. The pain perceived by the patients in these two categories may have been too severe to be alleviated by PD medication. Interestingly, when analyzing logistic regressions between the use of PD medication and pain severity, no significant relationships were found in patients reporting a direct effect of medication. Logistic regressions also revealed that the wearing off of PD medication has no effect on the magnitude of pain reported by patients. Although 18 of the 45 patients who were asked about their PD medication perceived that it had a direct effect on their pain symptoms, this was not reflected in the results and may indicate a placebo effect.

Compared with studies reported in the literature, the present study had a relatively large sample size and adopted a novel approach to the study of pain in the PD population. This approach, in addition to the standardized assessment methods used which limit any bias, is a significant strength of this study and was shown to be applicable to the study of PD-associated pain. Excluding patients with cognitive dysfunction and dementia also helped to ensure the validity of patient accounts throughout the interview process. Although large in comparison to some studies, our sample size is nevertheless a limitation of this study – indeed, due to the size of the sample, smaller groups had to be merged (i.e. the pain scale ratings, given on an ordinal range of 1-10, had to be considered in three broad categories). This may have resulted in a failure to detect changes between these groups. Furthermore, no age-matched controls were used in this study and as a result, a proper comparison between prevalence rates in PD and the general population could not be made.

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