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Disability from pain directly correlated with depression in Parkinson's disease

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ABSTRACT

Objective: Parkinson's disease (PD) is a progressively debilitating disorder resulting in reduced quality of life (QoL). Along with the motor symptoms of PD, non-motor symptoms of PD such as pain, restless leg syndrome (RLS) depression also occur. These exacerbate the worsening QoL and must be promptly diagnosed and treated. The objective of this study was to determine the relationship between pain severity, walking, general activity and work (WAW) and rapid eye movements (REM) dimensions of pain interference, and disability with depression and RLS in PD.

Patients & methods: 120 patients with PD and 120 controls were evaluated for depression using the Hospital Anxiety and Depression Scale (HADS-D). Pain severity and interference was measured using Brief Pain Inventory (BPI). REM and WAW dimensions of pain were also measured. The Pain Disability Index (PDI) was used to assess the disabling effects from chronic pain.

Results: The study found a statistically significant direct correlation between the BPI, PDI and PD. A significant direct correlation was also found for depression and pain in PD. No association as found between RLS and PD; RLS was not a confounding factor.

Conclusions: Based on these findings, we conclude that pain interference, severity of pain and disability from pain is directly correlated with depression in PD. We also discern that these symptoms of PD are not independent of each other. We cannot establish a causal relationship between any of these variables. Prompt recognition and treatment of pain and depression is valuable in preserving the quality of life in PD.

1. Introduction

Patients with Parkinson's disease (PD) experience motor, non-motor and neuropsychiatric manifestations that negatively impact their overall quality of life (QoL). PD is a chronic, progressively debilitating neurodegenerative disorder that affects between 0.1%–0.3% individuals and prevalence increasing with age [1]. The diagnostic features of PD are tremor, bradykinesia, and rigidity [2]. Non-motor symptoms (NMS) include pain and sensory disturbances, mood disorders including depression and sleep disturbances including Restless Leg Syndrome (RLS) [3–6]. The 2009 PRIAMO study of over 1070 PD patients found that 97% of patients reported NMS [3] of which pain, mood disorders, and sleep problems were of most concern [6].

Studies have consistently showed that up to 85% of patients with PD report pain [5] of which musculoskeletal (often caused by rigidity) and dystonic pain (caused by side effects of medication) were common [7,8]. Neuropathic pain (caused by neuropathy) and central pain (PD specific pain) are also common types of pain in PD patients [8]. NMS including pain are known to manifest before the triad of motor symptoms of PD [9]. Pain in patients with PD is often atypical, and is different from the pain experienced and expressed by patients without PD. Thus, pain is frequently neither recognized nor diagnosed in the early, premotor stages of PD [9] or when the diagnosis of PD has yet to be established. Further, pain can be understood in terms of interference, severity and disability. Pain interference hinders one's QoL as pain may impact social relationships, pleasure, mood and physical abilities [10].

Depression and anxiety commonly co-occur in PD and like pain, may present before the motor functions manifest [11] with depression being the most common psychiatric disturbance [12]. About 40–50% of patients with PD suffer from depression. While the causality between PD and depression is not well established, chronic pain and disruptions in sleep, in synergy with the rest of the motor and non-motor manifestations of PD can lead to depression. The finding that pain interference, severity, and disability was found to be higher in PD patients

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with depression supports this [13]. Because of the frequent co-occurrence of depression and pain in PD, a wide set of differentials including PD must be considered in patients with depression, pain and other risk factors.

Another NMS of PD is RLS. RLS is found in about 25% of the patients with PD [14]. The presence of RLS in PD is disputed – what presents as RLS may in fact be the adverse effect of the drugs used to treat PD, the 'wearing off' effect of PD medications, PD medications masking RLS [15], akathisia or tremors or simply "restlessness" [15]. Unlike the actual diagnosis of RLS, restlessness experienced by patients with PD is rather brief and is not as severe. Recent studies show that RLS may delay onset and progression of PD and reduce dyskinesia [16]. Another study found that both depression and anxiety were increased in PD with RLS, albeit the severity was not statistically significant [17]. In light of these findings, we intend to identify any correlation between PD and RLS.

Early detection and intervention of treatable NMS such as pain, depression and restlessness is paramount to the patient's QoL, as poor outcomes including disability, death, dementia or postural instability are likely to occur within 10 years [18]. Importance must be given to the possibility of PD as a differential diagnosis when assessing a patient with atypical pain and sensory alterations, restlessness and depression. Additionally, determining if early signs and symptoms of pain, depression and restlessness in addition to other NMS can be utilized as predictors of PD would help in earlier diagnosis and intervention in treating PD. Finally, a better comprehension of the variety of pain is crucial for healthcare providers to prescribe appropriate pharmaceutical and non-pharmaceutical therapies targeted towards the distinct pains experienced by patients with PD. Further research into correlation and causation of pain, depression and RLS in PD can be utilized to address the predictors of morbidity and mortality in PD.

The intent of this study is to examine the relationship between the NMS of pain, depression and RLS and PD. We further breakdown pain into interference caused by pain in daily activities and the severity of pain.

2. Materials and methods

2.1. Subjects and measures

PD patients were seen routinely (i.e. two to three times a year) at a community-based movement disorders clinic for their regular PD care and were randomly selected for this study. However, patients with dementia, atypical Parkinsonism or non-consenting patients were not included. Patients meeting criteria of this study were chosen in a consecutive manner. 120 patients with PD from community-based movement disorders clinic were included in this study. This group of patients included 82 males and 38 females of mean age 70.2 ± 11.0 years. Between June 2011–2012, these selected patients visited the PD clinic where assessment was conducted through semi-structured, non-consecutive interviews followed by a neurological examination. A control group 120 healthy individuals matching for age and gender were recruited from the similar demographics. This group consisted of healthy participants who accompanied the PD patients to their routine neurological assessments, but were not biologically related to the patient. The control group included 82 males and 38 females of mean age 69.4 ± 10.5 years who were randomly selected. More specifically, controls were chosen in a consecutive manner, similar to the patients. All selected individuals were assessed in a single visit through semi-structured, non-consecutive interviews followed by a complete neurological examination. Both PD patients and control groups consisted of age and gender matched participants.

PD was diagnosed according to the U.K. Brain Bank Criteria [19] and RLS was diagnosed according to the RLS Diagnostic Criteria [20]. The severity and caseness of depression (HADS-D) was assessed using the Hospital Anxiety and Depression Scale (HADS) [21] where a score greater or equal to 8 in the validated HADS indicated severity and caseness of depression. The Brief Pain Inventory (BPI) was used to assess pain severity and pain interference. Pain interference was further assessed using two dimensions. Firstly, the REM dimension assessed pain that interferes with relationships, enjoyment of life and mood. Secondly, the WAW dimension assessed pain that interferes with walking ability, general activity and normal work activity [10]. The Pain Disability Index (PDI) was used to assess the effects of chronic pain [22]. This study was approved by the local ethics board.

2.2. Statistical analysis

Statistical analysis was conducted in two stages. Firstly, we compared patients and the control group using two-tailed *t*-tests and chi-square tests. We then divided the patients into two groups based on a validated cut-off score of 8 or more [23] on the Depression Severity Score (HADS-D) of the HADS scale, and subsequently compared the two groups using two tailed *t*-tests and chi square tests. The "Caseness-DEP" group had a HADS-D score of 8 or more, while the "Normal-DEP" group had a HADS-D score of less than 8. The Caseness-DEP group contained 42 males and 23 females of mean age 71.2 ± 1.56 years, and the Normal-DEP group contained 40 males and 15 females of mean age 68.3 ± 1.90 years. Multiple logistic regression analysis was used to investigate if PDI, BPI, REM and WAW and depression was predicted by age, sex, age at diagnosis, prevalence of RLS, Hoehn and Yahr (H & Y) score, duration of disease, Unified Parkinson's disease rating scale part III 3 (UPDRS-III).

3. Results

3.1. Stage 1

Patients with PD scored 12, 4.7 and 9.5 points higher than controls on PDI, BPI pain severity and BPI pain interference BPI, respectively ($P < 0.0001$, $P < 0.0001$ and $P < 0.0001$). PD patients also scored 4.6 and 5.6 points higher than controls on the REM dimension and WAW dimension of BPI pain interference, respectively ($P < 0.0001$ and $P < 0.0001$) (Table 1). Compared to the control group, RLS was found in 19 of 120 patients with PD ($P < 0.0001$).

3.2. Stage 2

Caseness-DEP PD patients scored 10, 4.5 and 11 points higher than Normal-DEP PD patients on PDI, BPI pain severity and BPI pain interference respectively ($P = 0.008$, $P = 0.017$ and $P = 0.001$). Caseness-DEP PD patients also scored 5.0 and 5.9 points higher than Normal-DEP PD patients on the REM and WAW dimensions of BPI pain interference,

Table 1
Clinical correlates and key demographics of PD patients (n = 120) and/or controls (n = 120)§.

	PD Patients	Controls
Male:Female	82:38	82:38
Age	70.2 ± 11.0	69.4 ± 10.5
Age of diagnosis	66.3 ± 11.7	–
Disease duration	3.75 ± 4.24	–
H & Y score	2.35 ± 0.536	–
UPDRS-III score	24.2 ± 7.62	–
RLS ***	25	6
PDI-Global score ***	18.5 ± 21.6	6.53 ± 14.7
BPI-Global severity score ***	9.58 ± 10.4	4.93 ± 9.06
BPI-Global interference score ***	15.6 ± 18.9	6.1 ± 14.3
BPI-WAW Pain interference score ***	8.86 ± 10.8	3.27 ± 7.41
BPI-REM Pain interference score ***	6.69 ± 8.59	2.08 ± 5.34

§ Data is expressed as mean ± standard deviation, in counts or in ratio.
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.0001$.