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Increased likelihood of anxiety and poor sleep quality in Parkinson's disease patients with pain

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ABSTRACT

Background: Pain is a bothersome non-motor symptom in patients with Parkinson's disease (PD), but the relationships between PD, presence of pain, different pain characteristics, and other non-motor symptoms such as mood and sleep disturbances are unclear.
Objective: To investigate the relationship between PD and pain as well as specific subtypes of pain with anxiety, depression and sleep quality.
Methods: This cross-sectional case-control study included two groups of PD patients; one with ($n = 37$) and one without pain ($n = 37$). Healthy controls with ($n = 37$) and without pain ($n = 37$) were recruited and matched to the PD groups for age and gender. All participants completed questionnaires regarding pain, mood and sleep.
Results: PD patients with pain showed significantly higher anxiety severity and poorer sleep quality than PD patients without pain. Compared to controls with pain, PD patients with pain had more anxiety, depression and worsened sleep quality. PD patients with pain were more likely to report akathisic, tension and sharp pain compared to controls with pain, but these three pain characteristics did not correlate with each other. There were no differences in depression, anxiety, or sleep between PD patients with akathisic, tension and sharp pain and those without.
Conclusion: Pain in PD seems to be linked with specific pain characteristics (akathisic, tension and sharp pain) as well as heightened anxiety and worsened sleep quality. Integrative approach treatments which address pain in PD may also improve anxiety and sleep quality.

1. Introduction

Parkinson's disease (PD) is traditionally characterized as a motor disorder but it also has associated non-motor symptoms including disturbances in mood, cognition and sleep [1]. Literature on these non-motor symptoms also includes pain as a symptom associated with PD [2]. Pain is reported in over half (59.77%) of patients with PD [3], a higher frequency than in age- and sex-matched controls [4]. In a recent survey of PD patients, pain was the most bothersome non-motor symptom [4]. Despite this, there is little research in this area and the exact relationships between pain, PD, and other comorbid symptoms such as mood and sleep are not clearly established.

Insomnia, depression and anxiety are all common non-motor symptoms of PD [5–7]. Previous studies have extensively demonstrated distinct links between PD and separate variables such as pain [2], sleep disruptions [8], depression [9] and anxiety [10]. However, published research has yet to explore the relationship of the aforementioned factors to the association of pain with PD. Furthermore, pain, sleep disturbances, and mood disorders in the general population are often co-morbid [11], and it is not clear if the combination of pain and PD has an additive effect on mood and sleep.

It is also unclear if certain descriptors or characteristics of pain occur more in PD patients compared to controls. Research demonstrates the importance of assessing distinct pain domains and pain characteristics in clinical trials because this area of pain assessment has important implications for the patient [12].

In this study, participants included PD patients with and without pain, matched to healthy controls with and without pain. The purpose of this cross-sectional case-control study was threefold: 1) to determine the effect of the pain in PD on the individual symptoms of anxiety, depression and sleep quality, 2) to investigate if PD patients with pain were more likely to report certain pain characteristics compared to controls, and 3) to see if any of the significant pain characteristics identified correlate with mood or sleep quality.

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2. Methods

A total of 74 PD patients and 74 healthy controls were included in this cross-sectional case-control study. All PD patients met UK brain bank diagnostic criteria [8], and were recruited from a PD and movement disorders clinic over a period of one year (June 2011–June 2012). Patients with known atypical Parkinsonism and dementia were not included in the study. PD patients were categorized as having pain (PD(+)Pain) if they answered "yes" to a report of pain other than everyday kinds of pain on the Brief Pain Inventory (BPI) [9]. An equal number of healthy controls were recruited that matched the PD(+)Pain and PD groups for age, gender and pain frequency. Controls were participants who were biologically unrelated to the patients and accompanied the patients as recruits from various community centers, and had no past history of sleep or cognitive disorders. Questionnaires were administered using a semi-structured interview and a neurological examination was completed on all participants within 1–2 visits to the clinic by a movement disorders specialist. Informed consent was received from all participants after full disclosure of the study protocol. The study was reviewed and approved by the local ethics review board. Severity and frequency of pain was assessed using the BPI. Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) [10]. If the HADS-A score of a participant was greater than or equal to 8, a caseness count for anxiety was recorded, with a parallel procedure for depression caseness count using the HADS-D score [13]. The Pittsburgh Sleep Quality Index (PSQI) was used as an overall measure of sleep quality [14]. Additionally, the presence or absence of Restless Legs Syndrome (RLS) was determined using the RLS diagnostic criteria [15].

ANOVA with Games-Howell post hoc method was used for detecting any significant pair-wise comparisons in age, age of diagnosis, BPI pain severity, HADS-A anxiety severity, HADS-D depression severity, BPI pain severity and PSQI global across the four groups. The chi square test with Bonferroni correction was used to detect any significant pair-wise comparisons in anxiety caseness, depression caseness and RLS prevalence across the four groups.

The two groups which reported "yes" for pain (PD(+)Pain and Control(+)Pain) were then analyzed using multiple logistic regression analysis to determine whether pain and Parkinson's disease was correlated with any of the following pain characteristics of the BPI: radiating, aching, dull, tension, sharp, boring, penetrating, shooting, throbbing, burning, stabbing, cramping, paresthetic and akathisic. Subsequent multiple logistic regression analyses were done to determine whether significant predictors from the aforementioned regression correlate with each other. Finally, significant correlates from the second stage were compared for HADS-A anxiety severity, HADS-D depression severity and PSQI global using Kruskal-Wallis 1-way ANOVA with pairwise comparisons.

3. Results

The PD groups each comprised of 28 males and 9 females ($n = 37$), with a mean age 69.1 ± 10.9 years for the PD(+)Pain group and 72.1 ± 8.46 years for the PD(−)Pain group. The control groups were also comprised of 28 males and 9 females ($n = 37$), with a mean age of 71.0 ± 9.46 years for the Control(+)Pain group and 67.5 ± 11.7 years for the Control(−)Pain group. Compared to PD(−)Pain patients, PD(+)Pain patients had significantly higher BPI pain severity scores (13.1 ± 9.83 vs. 1.22 ± 4.54, $p < 0.0001$), significantly higher HADS-A anxiety severity scores (8.81 ± 5.76 vs. 4.51 ± 4.04, $p < 0.0001$) and poorer sleep quality based on PSQI global score (8.46 ± 3.21 vs. 6.11 ± 3.52, $p = 0.021$). Compared to the Control(+)Pain group, PD(+)Pain patients had more anxiety (HADS-A anxiety caseness 19 vs. 5, $p < 0.05$; HADS-A anxiety severity 8.81 ± 5.76 vs. 3.97 ± 3.38, $p < 0.0001$) more depression (HADS-D depression caseness 24 vs. 5, $p < 0.05$; HADS-D depression severity 9.43 ± 4.31 vs. 3.27 ± 3.11, $p < 0.0001$), and worsened sleep quality on PSQI global score (8.46 ± 3.21 vs. 5.70 ± 3.84, $p < 0.05$). There were no significant differences between groups in terms of UPDRS motor scores, H&Y stage or RLS prevalence.

3.1. PD and specific pain characteristics

PD(+)Pain patients were 8.4 times more likely to report tension pain ($p = 0.034$), 7.5 times more likely to report sharp pain ($p = 0.016$), and 19 times more likely to report akathisic pain ($p = 0.005$) compared with Control(+)Pain individuals. Pain and PD was not significantly predicted by any of the other pain characteristics (Table 2). The three types of pain found to be significant (tension, sharp, and akathisic) in the regression and did not correlate with each other. There were no differences in HADS-A, HADS-D or PSQI scores between PD patients with and without tension, akathisic and sharp pain (see Table 3) (See Table 1).

4. Discussion

Among various past studies on PD and pain, none have yet investigated the joint impact of pain in PD on depression, anxiety and sleep quality [2,8–10]. This gap in research initiated the present study. We found that PD patients with pain had greater anxiety and poorer sleep quality than PD patients without pain. PD patients with pain also had

Table 1
Demographic and clinical data for PD patients and controls divided by a "yes" or "no" answer for a report of pain on the Brief Pain Inventory (BPI) scale.

Parameter	PD(+)Pain $n = 37$ Mean ± SD or Y(N)	PD(−)Pain $n = 37$ Mean ± SD or Y(N)	Control + Pain $n = 37$ Mean ± SD or Y(N)	Control $n = 37$ Mean ± SD or Y(N)
Age	69.1 ± 10.9	72.1 ± 8.46	71.0 ± 9.46	67.5 ± 11.7
Age of diagnosis	65.3 ± 10.7	68.8 ± 10.3	–	–
Disease duration	3.12 ± 3.36	3.23 ± 3.79	–	–
UPDRS-III	25.4 ± 6.75	22.0 ± 8.95	–	–
H&Y	2.32 ± 0.592	2.32 ± 0.475	–	–
BPI pain severity^{***,II,III,V}	13.1 ± 9.83	1.22 ± 4.54	8.30 ± 9.74	0.487 ± 2.08
HADS-A anxiety caseness^{*,I,II,III,IV}	19 (18)	8 (29)	5 (32)	4 (33)
HADS-A anxiety severity^{***,I,II,V}	8.81 ± 5.76	4.51 ± 4.04	3.97 ± 3.38	2.70 ± 3.02
HADS-D depression caseness^{*,I,II,III,IV}	24 (13)	16 (21)	5 (32)	3 (34)
HADS-D depression severity^{***,I,II,III,IV}	9.43 ± 4.31	7.05 ± 3.62	3.27 ± 3.11	2.41 ± 3.24
PSQI global^{**I,***II,*IV,*V}	8.46 ± 3.21	6.11 ± 3.52	5.70 ± 3.84	3.78 ± 3.22
RLS prevalence	8 (29)	2 (36)	2 (36)	3 (34)

^{I} = PD(+)Pain vs. Control + Pain; ^{II} = PD(+)Pain vs. Control;
^{III} = PD(−)Pain vs. Control + Pain; ^{IV} = PD(−)Pain vs. Control; ^{V} = PD(+)Pain vs. PD(−)Pain.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.0001$.