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Axial postural abnormalities and pain in Parkinson's disease

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Abstract

Axial postural abnormalities and pain are two main determinants of poor quality of life in patients with Parkinson's disease (PD). Indeed, a detailed characterization of pain and other non-motor symptoms in patients with PAs has not been provided yet. The aim of this study is to assess the phenomenology of pain and other non-motor symptoms in PD patients with Pisa syndrome and camptocormia compared to PD patients without axial postural abnormality. Forty-five PD participants were equally distributed in three groups: patients with Pisa syndrome (PS), patients with Camptocormia (CC), and patients without postural abnormalities (PD). Pain characteristics were assessed by Kings Parkinson's Pain Scale (KPPS), brief pain inventory (BPI), and numeric pain rating scale (NRS). All participants completed clinical assessments by non-motor symptom scale (NMSS), and movement disorder society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) parts II–III. Patients with and without axial postural abnormalities showed one or more types of pain, being fluctuation, nocturnal, chronic, and musculoskeletal the most frequently reported in Pisa Syndrome and camptocormia. PD group compared with PS and CC groups showed differences in the KPPS, NMSS, BPI pain severity and interference, and NRS total scores. No significant differences were found between PS group compared with CC group with exception of the NMSS total scores. PD patients with Pisa syndrome or camptocormia have a higher burden of musculoskeletal, chronic and fluctuation pain than PD patients without axial postural abnormalities, suggesting different etiologies of pain and possible different treatments.

Keywords Axial postural abnormalities · Pisa syndrome · Camptocormia · Pain · Parkinson's disease · Physiotherapy

Introduction

Axial postural abnormalities such as Pisa syndrome, antecollis, and camptocormia are common disabling motor features of advanced Parkinson's disease (PD), affecting nearly 20% of patients (Doherty et al. 2011; Tinazzi et al. 2019a, 2022). Occurrence of axial postural abnormalities (Doherty et al. 2011; Tinazzi et al. 2019b) has a major negative effect in patient's motor function (i.e., mobility) leading to disability and poor quality of life (Geroin et al. 2015, 2020; Alwardat et al. 2018, 2019a; Buhmann et al. 2020). Another main determinant of significant disability and poor quality of life in PD (Beiske et al. 2009) is pain, which is frequent (Tai and Lin 2020; Tinazzi et al. 2022), and appears at any time during the disease course. Up to 85% of PD patients suffer from different types of pain such as musculoskeletal, neuropathic, dystonic, central and visceral chronic, and orofacial pain (Marques and Brefel-Courbon 2021).

Both, axial postural abnormalities and pain represent two critical aspects of patients' well-being, whose underlying

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pathophysiological mechanism is unclear along with their therapeutic management (Antonini and Tinazzi 2015). Of interest, the coexistence of axial postural abnormalities and pain in PD has been recognized by several studies (Geroin et al. 2015; Alwardat et al. 2019a, b; Tinazzi et al. 2019b), but none provided a detailed characterization of pain phenomenology in different categories of axial postural abnormalities, which instead is fundamental to customize effective therapeutic interventions. In fact, the identification of pain characteristics may help to develop specific therapeutic pharmacological (i.e., botulinum toxin) and non-pharmacological strategies (i.e., physiotherapy) for its management (Antonini and Tinazzi 2015). A detailed assessment of nociceptive inputs and pain mechanisms is essential to guide tailored etiological therapy, which may differ from patient to patient. Therefore, a better understanding of pain phenotypes is critical to guide interventions to ensure pain relief, improved patient recovery and quality of life.

Indeed, King's Parkinson disease Pain Scale (KPPS) (Chaudhuri et al. 2015) is a newly introduced clinical scale allowing detailed assessment of pain in PD patients. To the best of our knowledge, no studies have been published so far on pain evaluated by KPPS in Pisa Syndrome and camptocormia. Here, we used KPPS and other clinimetric tools to investigate pain characteristics in PD patients with Pisa syndrome and camptocormia, compared to PD patients without axial postural abnormalities, to identify those elements that may support clinical management of such a vulnerable category of patients.

Materials and methods

Study design

This is a pilot observational cross-sectional study involving 45 patients distributed in three groups: 15 patients with PD and camptocormia (CC) with upper fulcrum (the bending angle at a point between the lower thoracic and upper lumbar spine) (Tinazzi et al. 2022) 15 patients with PD and Pisa syndrome (PS) (Tinazzi et al. 2022) and 15 patients with PD but without postural abnormalities (PD). Patients were recruited consecutively to reach the number of 15 each group. All patients were attending the outpatient clinic of the Movement Disorders Division, Neurology Unit of Policlinico Tor Vergata (Rome, Italy).

Patients

All patients underwent neurological evaluation by a neurologist expert in movement disorders before their enrollment. Inclusion criteria were: a medical diagnosis of PD confirmed according to the MDS clinical diagnostic criteria (Postuma et al. 2015); Camptocormia with thoracic fulcrum (C7–T12 vertebrae), measured with a wall goniometer, defined as $\geq 45°$ thoracolumbar flexion apparent when standing or walking but resolving when the patient lies supine (Tinazzi et al. 2022); and PS was defined as $\geq 10°$ of lateral trunk flexion, measured with the wall goniometer, that can be reduced by passive mobilization or supine positioning (Tinazzi et al. 2022); a history of pain for at least 12 weeks; walking ability for a short distance (10 m) without use of assistive device. Exclusion criteria were: severe dyskinesia or "on–off" fluctuations to exclude patients with painful off-dystonia; modified Hoehn & Yahr (mH&Y) stage > 3 in "ON" medication phase, cognitive impairment scored with the Mini-Mental status Examination (MMSE) < 24, PD medication modification in the 3 months preceding enrollment into the study; the need of assistive devices to rise from a chair or bed; the presence of other neurological, orthopedic (i.e., scoliosis) or cardiovascular co-morbidities; and patients had received spinal surgery. All patients gave their informed consent to participate in the study. The study was carried out according to the Declaration of Helsinki and was approved by the Local Ethics Committee (Protocol 212/16).

Assessment procedures

Clinical data and assessments were collected through a standardized personal interview with the patients on their usual drug treatment during the ON medication phase; all patients were on best medical treatment. We recorded the following clinical and demographic variables: gender, age, weight, height and body mass index (BMI), PD duration, disease severity assessed using the movement disorder society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part II (activities of daily living) and part III (motor performance) (Goetz et al. 2008), staging of the disease determined using the Modified Hoehn and Yahr staging scale (H&Y) (Hoehn and Yahr 2001), and the levodopa equivalent daily dose (LEDD) calculated using standardized conversion formulas (Tomlinson et al. 2010). Cognitive impairment was evaluated with the mini-mental state examination with the score adjusted for age and educational level (Folstein et al. 1975).

The primary outcome measure was the Kings Parkinson's Pain Scale (KPPS). An Italian version of the KPPS was used to identify and grade the various types of pain (Chaudhuri et al. 2015). It is a specific pain scale used to evaluate the characterization of various pain phenotypes of pain in individuals with PD. KPPS has seven domains including 14 items that evaluate different pain characteristics and phenotypes include (musculoskeletal pain, chronic pain, discoloration, edema/swelling, fluctuation-related pain, nocturnal pain, orofacial pain, radicular pain). Each item is scored by severity (0, none to 3, very severe) multiplied by frequency

(0, never to 4, all the time) resulting in a sub-score of 0–12, the sum of which gives the total score with a theoretical range from 0 to 168.

Secondary outcome measures were pain severity and interference evaluated according to the Italian version of the Brief Pain Inventory (BPI) (Caraceni et al. 1996). The responses to each item on this self-administered questionnaire are graded on an 11-point NRS from 0 (no pain / no interference) to 10 (worst pain / complete interference) (Caraceni et al. 1996). Pain intensity was also assessed by means of the 11-point NRS, where 0 indicates no pain, 1–3 mild pain, 4–6 moderate pain, and 7–10 severe pain (Perez-Lloret et al. 2016). Non-motor symptom scale (NMSS) includes nine domains and 30 items (Chaudhuri and Martinez-Martin 2008). An Italian version of the NMSS was used to evaluate the severity of non-motor symptoms (Cova et al. 2017).

Statistical analysis

Descriptive statistics included frequency tables and calculation of means and standard deviation. Normal distribution was checked using the Shapiro–Wilk test. Non-parametric or parametric test were calculated accordingly. Demographical and clinical characteristics of the patients (age, BMI, disease duration, NMS total scores, MDS-UPDRS II and III scores, H&Y stage, LEDD, and MMSE were analyzed with non-parametric Kruskal–Wallis *H* test. We compared the groups using the Chi-squared test or Fisher's exact test (if ≤ 5 expected frequencies) for categorical variables. The primary (KPPS) and secondary outcomes (BPI, NRS, and NMS) were analyzed using one-way analysis of variance (ANOVA), with between factor the "Groups" (CC, PS, PD) as independent variables and within factor the total scores of each outcome. Post hoc comparisons were performed using Tukey's multiple comparison test to evaluate whether there was any difference among the three groups after adjusting for multiple testing. To compare the KPPS and NMS domains scores between the three groups, analysis of covariance (ANCOVA) was conducted, adjusted for potential confounding factors (H&Y staging, MDS-UPDRS-III, LEDD and disease duration). Statistical analyses were carried out using the IBM® SPSS® Statistics version 22.0 for Macintosh.

Results

Demographical, clinical characteristics of patients and body distribution of pain

The demographical and clinical characteristics of the three groups are presented in Table 1. All patients were receiving chronic therapy with a dopaminergic drug and showed good motor compensation in appendicular function. None had psychiatric disturbances or cognitive impairments were observed. Patients with and without axial postural abnormalities showed one or more types of pain, according to KPPS score (Fig. 1). Fluctuation, nocturnal and musculoskeletal were the most frequent types of pain reported in patients with PS. Nocturnal, chronic and musculoskeletal were the most frequent types of pain reported in patients with CC. Patients without PA present equally distributed different types of pain (Fig. 1). In PS group, pain was localized in the lumbar spine in 5 patients; cervical and lumbar spine and right leg in 5 patients; lumbar spine and left leg in 2 patients; in the cervical spine and lumbar spine in 3 patients. In CC group, pain was localized in the

Table 1 Demographical and clinical characteristics of the patients

	Total	PD	PS	CC	*P* Value
Patients. no,	45	15	15	15	–
Gender M/F	30/15	10/5	10/5	10/5	0.819
Age, mean (SD), yrs	65.58 (5.79)	65.47 (2.17)	65.60 (3.98)	65.67 (9.22)	0.901
BMI (Kg/M^2)	26.17 (3.80)	25.73 (3.78)	25.84 (3.79)	26.94 (4)	0.699
Disease duration, yrs	5.4 (3.16)	3.13 (1.92)	6.73 (2.63)	6.33 (3.54)	**0.002**
UPDRS II score	12.57 (5.29)	6.27 (1.92)	15 (2.93)	16.47 (2.97)	**< 0.001**
UPDRS-III score	31.51 (10.17)	20.87 (4.98)	34.87 (7.74)	38.80 (7.10)	**< 0.001**
H&Y stage	2.43 (0.60)	1.70 (0.41)	2.77 (0.26)	2.83 (0.24)	**< 0.001**
LEDD (mg/day)	582.02 (282.07)	358 (203.37)	673.53 (185.63)	714.53 (304.45)	**< 0.001**
MMSE (0–30)	26.72 (1.82)	28.14 (1.73)	25.37 (1.16)	26.62 (1.43)	**< 0.001**

PD denotes patients with Parkinson's (without Pisa or camptocormia), *PS* denotes patients with Parkinson's disease and Pisa syndrome, *CC* denotes patients with Parkinson's disease and camptocormia, *SD* standard deviation, *M* male, *F* female, *yrs* years, *H&Y* stage Hoehn and Yahr stage, *UPDRS* Unified Parkinson's Disease Rating Scale, *BMI* body mass index, *LEDD* Levodopa equivalent daily dose, *MMSE* minimental status evaluation

P significant if < 0.05 in bold

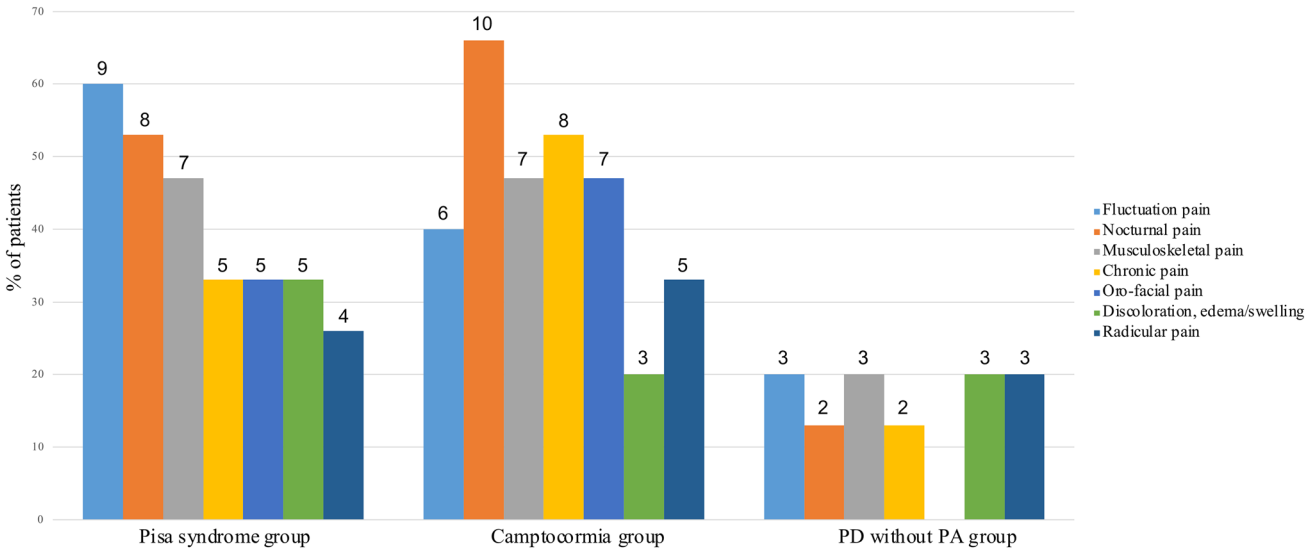

Fig. 1 Absolute frequency (and percentage) of PD patients with Pisa syndrome, camptocormia, and without axial postural abnormalities presenting one or more type of pain according to the King Parkinson's pain scale

cervical spine and right and left shoulder in 6 patients; lumbar and cervical spine and right and left shoulder in 4 patients; only in the cervical spine in 3 patients; in the lumbar and cervical spine in 2 patients (Fig. 2).

No significant differences in age, gender and BMI were found between the three groups (Table 1).

Patients with PS and CC had longer disease duration, higher score in the MDS-UPDRS II and III, H&Y stage, LEDD, but a lower score of MMSE than patients without PA (Table 1). No differences were found in H&Y, LEDD, disease duration, MDS-UPDRS II and III, and MMSE between patients with PS and CC.

Primary outcome

A significant main effect in the KPPS total scores was found between the three groups ($F = 29.16$; df = 2, $P < 0.001$). The mean KPPS total scores were higher in PS group compared to CC group (45, 42.52; respectively). Post hoc comparison revealed a significant difference in KPPS total scores between PD group (10.80) compared with PS (45) and CC (42.52) groups, respectively ($P < 0.001$, $P = 0.005$), and no significant difference was found in KPPS total scores between PS group compared with CC ($P = 0.875$).

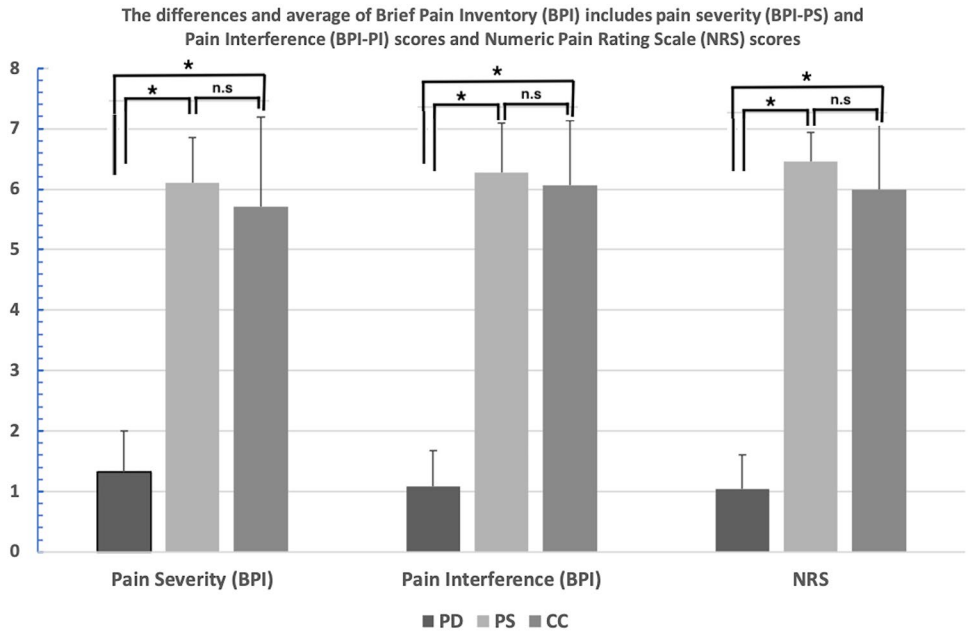

Fig. 2 The differences and average of brief pain inventory (bpi) includes pain severity (bpi-ps) and pain interference (BPI-PI) scores and numeric pain rating scale (NRS) scores, represent as (Mean ± SD) in *PD* patients with Parkinson's disease (without postural abnormalities), *PS* patients with Parkinson's disease and Pisa syndrome and *CC* denotes patients with Parkinson's disease and camptocormia. The significance values are reported (*$P < 0.05$)

ANCOVA test showed a significant difference in the mean sub-domains score of KPPS between the three groups in the musculoskeletal pain, chronic pain and fluctuation-related pain domains, independently from H&Y staging, MDS-UPDRS-III, LEED, and disease duration, respectively ($P=0.01$, $P=0.02$, $P=0.02$) (Table 2). The mean scores of fluctuations related pain domain was significantly higher in the PS group (10.46) compared to PD and CC ($P=0.02$), and the remaining domains of KPPS were similar or equal in three groups (Table 2).

Secondary outcomes

A significant main effect in the NMS total scores was found between the three groups ($F=21$; df = 2, $P<0.001$). Post hoc comparison revealed a significant difference in NMS total scores between PD group compared with PS and CC groups, respectively ($P<0.001$, $P=0.005$), and a significant difference was found in NMS total scores between PS group compared with CC ($P=0.008$). ANCOVA test revealed a significant difference in the mean domains score of NMS between the three groups in the mood/apathy, attention/memory, sexual dysfunction and miscellaneous domains, independently from H&Y staging, MDS-UPDRS-III, LEED, and disease duration. (Table 2). The mean scores of the mood/apathy domain were significantly higher in CC group compared to PD and PS ($P<0.001$) (Table 2). The mean scores of the attention/memory domain were significantly higher in PS group compared to PD and CC group ($P<0.001$) (Table 2). In addition, the mean scores of attention/memory, sexual dysfunction, and miscellaneous domains were significantly higher in PS group compared to PD and CC, respectively ($P=0.03$, $P<0.001$, and $P=0.03$). The scores of the remaining domains of NMS were similar or equal in three groups (Table 2).

BPI-SF pain severity showed a significant main effect between the three groups ($F=97.33$; df = 2, $P<0.001$) (Fig. 1). The mean pain severity scores were higher in PS group (6.1) and CC group (5.71), and lower in PD group (1.33). Post hoc comparison revealed a significant difference in BPI-SF pain severity between PD group compared with PS and CC groups, respectively ($P<0.001$, $P<0.001$), and no significant difference was found in BPI-SF pain severity between PS group compared with CC ($P=0.562$). BPI-SF pain interference showed a significant main effect between the three groups ($F=129.30$; df = 2, $P<0.001$) (Fig. 1).

Table 2 Comparisons of the primary and secondary outcome measures between the three groups

	PD	PS	CC	*P* Value
Primary outcome measure				
KPPS scale				
KPPS total scores	10.80 (3.70)	45 (20.87)	42.52 (10.56)	**< 0.001**
Musculoskeletal pain	1.66 (1.11)	6.26 (4.77)	6.20 (4.08)	**0.01**
Chronic pain	1.73 (0.88)	6.93 (7.35)	6.26 (4.39)	**0.04**
Fluctuation related pain	1.93 (1.27)	10.46 (7.79)	6.86 (4.86)	**0.02**
Nocturnal pain	1.53 (0.91)	8.33 (7.29)	9.40 (6.13)	0.334
Oro-facial pain	1.60 (1.12)	4.66 (5.87)	5.80 (5.26)	0.711
Discoloration, edema/swelling	1.33 (1.04)	4.86 (5.16)	3.86 (4.74)	0.254
Radicular pain	1.06 (1.16)	3.73 (2.89)	4.13 (3.22)	0.232
Secondary outcome measure				
NMS total scores	41 (18.34)	118.66 (42.14)	80.86 (33.46)	**< 0.001**
Cardiovascular	1.73 (2.6)	4.66 (3.22)	3.26 (2.93)	0.340
Sleep/fatigue	6.33 (6.18)	17.60 (14.02)	13.33 (11.34)	0.145
Mood/apathy	7 (5.18)	11.53 (11.77)	14.42 (13.64)	**< 0.001**
Perceptual problems/hallucinations	1.06 (3.03)	6.26 (5.39)	3.57 (4.42)	0.090
Attention/memory	4.46 (4.25)	13.13 (7.48)	7.60 (7.04)	**0.03**
Gastrointestinal	3.33 (4.62)	11 (6.77)	7.95 (7.03)	0.454
Urinary	6.26 (4.68)	14.66 (11.16)	15.73 (13.69)	0.957
Sexual dysfunction	3.63 (4.64)	12.86 (5.86)	7.20 (6.42)	**< 0.001**
Miscellaneous	6.33 (5.67)	14.53 (6.05)	9.26 (7.70)	**0.03**

KPPS King's Parkinson's Disease Pain Scale (KPPS), *NMS* non-motor symptoms scale, *NRS* numerical rating scale, *PD* patients with Parkinson's disease (without postural abnormalities), *PS* patients with Parkinson's disease and Pisa syndrome and *CC* denotes patients with Parkinson's disease and camptocormia

P value is calculated from ANCOVA with adjustment for H&Y staging, LEDD, UPDRS-III, and disease duration

Bold indicates statistical significance

The mean pain interference scores were equal in PS and CC groups (6.27, 6.07), respectively, and lower in PD group (1.09). Post hoc comparison revealed a significant difference in BPI-SF pain interference between PD group compared with PS and CC groups, respectively ($P<0.001$, $P<0.001$), and no significant difference was found in BPI-SF pain interference between PS group compared with CC ($P=0.798$) (Fig. 1).

NRS scores showed a significant main effect between the three groups ($F=220.682$; df = 2, $P<0.001$) (Fig. 1). The mean pain intensity scores were equal in PS and CC groups (6.46, 6), respectively, and lower in PD group (1.04). Post hoc comparison revealed a significant difference in NRS scores between PD group compared with PS and CC groups, respectively ($P<0.001$, $P<0.001$), and no significant difference was found in NRS scores between PS group compared with CC ($P=0.244$) (Fig. 1).

Discussion

Our results seem to indicate that PD patients with Pisa Syndrome or camptocormia have higher burden of pain than PD patients without axial postural abnormalities, as evaluated by a specific pain scale for PD. The burden (severity and frequency) of musculoskeletal, chronic and fluctuation pain were higher in patients with axial postural abnormalities than in patients without. Patients with camptocormia and Pisa syndrome were also affected by a higher intensity of pain and interference in mobility and activity of daily living (i.e., walking, sleeping, social activities) than patients without axial postural abnormalities. Moreover, pain localization in PD patients with axial postural abnormalities was mainly localized in the lower back (thoracic and lumber region), and lower limbs in Pisa syndrome and in the neck (cervical and thoracic regions) and upper limb (shoulder and scapular region) in camptocormia patients, whereas PD patients without postural abnormalities did not show such a prevalent localization of pain. These data suggest that pain can be generated and aggravated by postural abnormalities, and this may underpin the potential different etiologies of pain in axial postural abnormalities.

Musculoskeletal pain is one of the most frequent types of pain in patients with PD (Defazio et al. 2017; Fu et al. 2018), originating from muscles and joints disorders including kyphoscoliosis, camptocormia, Pisa syndrome, antecollis, bone mineralization disorders (e.g., osteoporosis and bone fractures), osteoarthritis (Rabin et al. 2016; Rana et al. 2018), humeral-acromial impingement syndrome and capsulitis. These disorders cause inflammation (i.e., bursa inflammation and shoulder pain), a gradual restriction in the range of motion (Papalia et al. 2019), and spontaneous onset of pain. More than 50% of patients with PD report chronic low back pain (Galazky et al. 2018) but whether this is from peripheral origin (nociceptive pain) or centrally maintained (primary low back pain) are still a matter of investigation. Peripheral driven lower back pain can be caused by muscular imbalances inherent to a movement disorder and by skeletal degeneration. Camptocormia and Pisa Syndrome patients present postural and gait impairments as they exhibit wider base of support, reduced swing time, marked reduction in range of motion of the lower extremity joints, and abnormal hip and pelvic pattern during the movement (Tramonti et al. 2017; Geroin et al. 2019; Do Nascimento et al. 2021). The abnormal biomechanical consequences lead to asymmetric weight bearing in the lower extremity that could increase axial postural deformities and pain (Geroin et al. 2019). Axial postural abnormalities can interfere with the overall load on the musculoskeletal system, and therefore cause muscle contractions and inflamed joints and tendons, especially in the lower back. In this view, the significantly higher intensity of pain referred by Pisa Syndrome and camptocormia patients may suggest a musculoskeletal origin of pain.

Our findings also emphasize the role of central mechanisms in aggravating pain symptoms in patients with axial postural abnormalities. Painful dystonia develops in approximately one-third of patients with PD that receive long-term levodopa treatments (Kodama et al. 2011). Previous studies have shown that the prevalence of dystonia-related pain ranges from 8 to 50% in patients with PD (Tinazzi et al. 2006; Kodama et al. 2011; Lin et al. 2013). In our sample of patients, painful dystonia can be the result of hyperactivity of the paraspinal (ipsilateral and contralateral) and non-paraspinal muscles. In Pisa Syndrome, pain can be the result or aggravated by the hyperactivity of muscles ipsilateral to the side of flexion or contralateral excessive muscle activation which may be a compensatory mechanism (Tinazzi et al. 2013). In patients with camptocormia, pain can be the result of hyperactivity of bilateral abdominal internal and external oblique together with rectus abdominis and iliopsoas muscles (Furusawa et al. 2015; Margraf et al. 2017). The evidence of a dystonic activity of non-paraspinal muscles is supported by the improvement of pain and camptocormia after the injection of lidocaine in the oblique external muscle (Furusawa et al. 2015). In a recent study, 452 PD patients were assessed for pain regardless of their ON or OFF status, and optimization of levodopa therapy reduced pain by at least 30% on the NRS score in 82.52% of patients (Li et al. 2022). In our series, patients were evaluated in their best ON therapy, suggesting that a dystonic pain responsive to levodopa was unlikely. Nevertheless, there is evidence that Pisa syndrome patients exhibit more severe form of dyskinesia and dystonia (Barone et al. 2016), hence our finding that fluctuation pain was prevalent in PS group deserves further and focused investigation in a larger sample. It's important to

mention that only camptocormia with thoracic fulcrum was included in this study. There is the possibility that patients with lumbar camptocormia have even a higher pain load. Thus, the future studies are recommended to investigate pain characteristics in camptocormia in both thoracic and lumbar fulcrum.

We found that NMSS domains scores including mood/apathy, attention/memory were higher and significantly worse in PS and CC groups compared to PD group. Pain is strictly related to other non-motor symptoms, including fatigue, daytime sleepiness, depression, and sleep disorders (Ozturk et al. 2017). Patients with PD that displayed depressive symptoms had significantly higher pain severity and pain interference scores than controls without depressive symptoms (Cruz-Almeida et al. 2020). The NMS scale showed a correlation between pain and attention/memory (Okada et al. 2016) which is in line with our findings. We did not find difference in other non-motor symptoms, like sleep and autonomic symptoms, which have, however, positive association in other studies. Thus, the role of Non-Motor Symptoms in pain perception should be specifically addressed in the Pisa Syndrome and the Camptocormia population in a study specifically designed for this outcome.

The pathophysiological mechanisms underlying pain in PD are not fully understood and therapeutic management remains a challenge (Antonini and Tinazzi 2015; Antonini et al. 2018). Several subtypes of pain have been described in PD, including musculoskeletal, neuropathic, dystonic and, less frequently, nocturnal, central and visceral chronic, discoloration/ edema/swelling and orofacial pain (Defazio et al. 2008; Wasner and Deuschl 2012; Antonini and Tinazzi 2015; Antonini et al. 2018). Abnormal nociceptive input processing in the central nervous system (CNS) leading to hypersensitivity to evoked pain probably underlies the different types of (spontaneous) pain experienced by PD patients and by pain-free PD patients (Zambito-Marsala et al. 2017). Neurodegeneration involving the non-dopaminergic systems (e.g., γ-aminobutyric acid, glutamate, noradrenaline, and serotonin) that modulate pain processing in other regions of the CNS may also play a relevant role (Wasner and Deuschl 2012; Tinazzi et al. 2013).

As pain processing involves brain regions that adapt to chronic pain states by engaging regions critical for cognitive/emotional assessments (namely prefrontal and anterior cingulate cortex—PFC/ACC) (Apkarian et al. 2005), we can speculate that central mechanism may coexist in our population and may alter pain perception in patients that display more severe modification in cognitive and emotional items such as attention and mood on the NMS evaluation. Consistent with this hypothesis, NMS domain mood/apathy were higher in Pisa syndrome and camptocormia patients in our series, and this could be part of a picture in which endogenous pain modulatory systems, mood and motivational systems may be dysfunctional as a consequence of the monoamines depletion that has been described in both in PD patients and in chronic pain states. Genetic factors can modulate pain perception and susceptibility in PD (Naureen et al. 2020). Additional factors (e.g., female sex, depression, disease duration, motor complications, postural abnormalities) and medical conditions (osteoporosis, rheumatic or degenerative joint disease) could contribute to the quality and spread of spontaneous pain (Wasner and Deuschl 2012). In this context, pain of different etiologies can be aggravated by axial postural abnormalities.

This study has several limitations. First, only the limited number of patients deserves for studies with a larger sample. In addition, we included PD patients with H&Y stage < 3, without relevant cognitive impairment (MMSE ≤ 24 was an exclusion criterion) and without severe dyskinesia. These criteria make the enrolled cohort a specific subset of PD population. Second, due to consecutive enrollment, the three groups were not well matched (age and gender). Nevertheless, results are not influenced by major confounders. Third, a more comprehensive assessment of pain in this population should investigate pain thresholds, beyond subjective pain self-evaluation. Moreover, pain should be evaluated according to muscle activation patterns in Pisa syndrome and camptocormia. Fourth, the role of non-motor symptoms as confounders should be specifically addressed in these populations. Fifth, the relation between the degree of trunk flexion and the severity of pain is not investigated. Thus, future studies are recommended to investigate this relation. Finally, the pain assessment was at on-medication. Further study should assess objectively the pain at on and off-medication status. Besides limitations, we recommend that the clinical assessment of pain in PD patients with postural abnormalities includes a thorough evaluation of possible pain mechanisms in order to account for variability of pain types in this population. Pain should be reassessed while monitoring PD progression and the efficacy of therapeutic interventions should be questioned at each follow-up. Future clinical trials might specify the change of different pain types rather than self-reported pain intensity.

In conclusion, PD patients with Pisa syndrome or camptocormia have a higher pain scores than PD patients without axial postural abnormalities. The burden of musculoskeletal, chronic and fluctuation pain was higher in patients with axial postural abnormalities, suggesting that pain can be of different etiologies and may need different treatments.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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