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RESEARCH ARTICLE

King's Parkinson's Disease Pain Scale, The First Scale for Pain in PD: An International Validation

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ABSTRACT: Pain is a key unmet need and a major aspect of non-motor symptoms of Parkinson's disease (PD). No specific validated scales exist to identify and grade the various types of pain in PD. We report an international, cross-sectional, open, multicenter, one-point-in-time evaluation with retest study of the first PD-specific pain scale, the King's PD Pain Scale. Its seven domains include 14 items, each item scored by severity (0-3) multiplied by frequency (0-4), resulting in a subscore of 0 to 12, with a total possible score range from 0 to 168. One hundred seventy-eight PD patients with otherwise unexplained pain (age [mean ± SD], 64.38 ± 11.38 y [range, 29-85]; 62.92% male; duration of disease, 5.40 ± 4.93 y) and 83 nonspousal non-PD controls, matched by age (64.25 ± 11.10 y) and sex (61.45% males) were studied. No missing data were noted, and floor effect was observed in all domains. The difference between mean and median King's PD Pain Scale total score was less than 10% of the maximum observed value. Skewness was marginally high (1.48 for patients). Factor analysis showed four factors in the King's PD Pain Scale, explaining 57% of the variance (Kaiser-Mayer-Olkin, 0.73; sphericity test). Cronbach's alpha was 0.78, item-total correlation mean value 0.40, and item homogeneity 0.22. Correlation coefficients of the King's PD Pain Scale domains and total score with other pain measures were high. Correlation with the Scale for Outcomes in PD-Motor, Non-Motor Symptoms Scale total score, and quality of life measures was high. The King's PD Pain Scale seems to be a reliable and valid scale for grade rating of various types of pain in PD. © 2015 International Parkinson and Movement Disorder Society

Key Words: Pain; Parkinson's disease; scale

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Pain is a frequent yet poorly understood non-motor symptom (NMS) of Parkinson's disease (PD), a key determinant of quality of life[1,2] and recognized by James Parkinson himself.[3] Pain in PD is heterogeneous and can be multifactorial in origin.[4] Various attempts of classification of pain exist based on cause (nociceptive vs. neuropathic pain), origin, location, and chronicity.[4,5] Prevalence data of pain from epidemiological studies report a wide variation, quoting rates ranging from 30% to 83%, largely owing to the lack of a validated instrument to assess pain in PD in clinical practice.[6] The latter issue also may explain why pain remains undeclared in 40.5% of PD patients when up to 80% of PD patients experience chronic pain.[4,7]

In this study, we present validation data from the first ever specific PD pain scale (King's PD Pain Scale [KPPS]) from a multicenter European field study.

Methods

Design

This was an international, cross-sectional, open, multicenter, one point-in-time evaluation with re-test study.

Patients and Consent

Parkinson's patients satisfying the UK PD Brain Bank criteria for diagnosis of idiopathic PD were invited to participate after informed consent if they had pain, as declared in item 10 of the NMS questionnaire (NMSQuest).[7] Exclusion criteria comprised:

a. Alternative or uncertain diagnosis of Parkinson's or drug-induced Parkinsonism
b. Inability to give consent
c. Dementia (formally diagnosed following internationally accepted criteria)
d. Diagnosis of disorders causing pain unrelated to PD (eg, severe osteoarthritis/arthritis, malignancy)

Sample Size

Prevalence of PD pain has previously been reported as 30% to 40% of PD patients. The sample size was calculated using baseline data from NMS Quest and NMS Scale (NMSS) studies, which report pain in 30% to 40% of patients (pain is a self-declaration item in NMSQuest and rated by severity and frequency in NMSS).[7,8]

Because the KPPS has 14 items, and following the recommended subject-to-item ratio of 10:1, a minimum number of 140 patients was required for the field validation. This sample size was increased by 15% to 160 to cover for missing data, input errors, and observer variability.

We estimated a ratio of patients to controls of 2:1.

Assessments

The KPPS is a rater-interview–based scale with the patient (aided by the carer if needed). Item generation was based on the advice of pain specialists, PD nurse specialists, and clinical advice from the PD Non-Motor Group (PDNMG) and the International Parkinson's and Movement Disorder Society (IPMDS) Non-Motor PD Study Group. In addition, we considered more than 500 patient responses related to pain items in NMSQuest and NMSS as well as a specific analysis of responses in relation to pain-related questions from a local study[9] (Fig. 1). The final structure of the scale was based on the Chaudhuri-Schapira classification of pain in PD (used in the PANDA study, OXN2504, ClinicalTrials.gov number NCT01439100) as well as classifications proposed by Wasner and Deuschl,[5] Negre-Pages et al.,[10] Tinazzi et al.,[11] and Ford.[4] The structure and the content of the scale was also reviewed and approved by an accredited Parkinson's expert patient group.

The final scale thus addresses localization, intensity, and frequency of pain as well as its relationship with motor fluctuations or musculoskeletal pain.

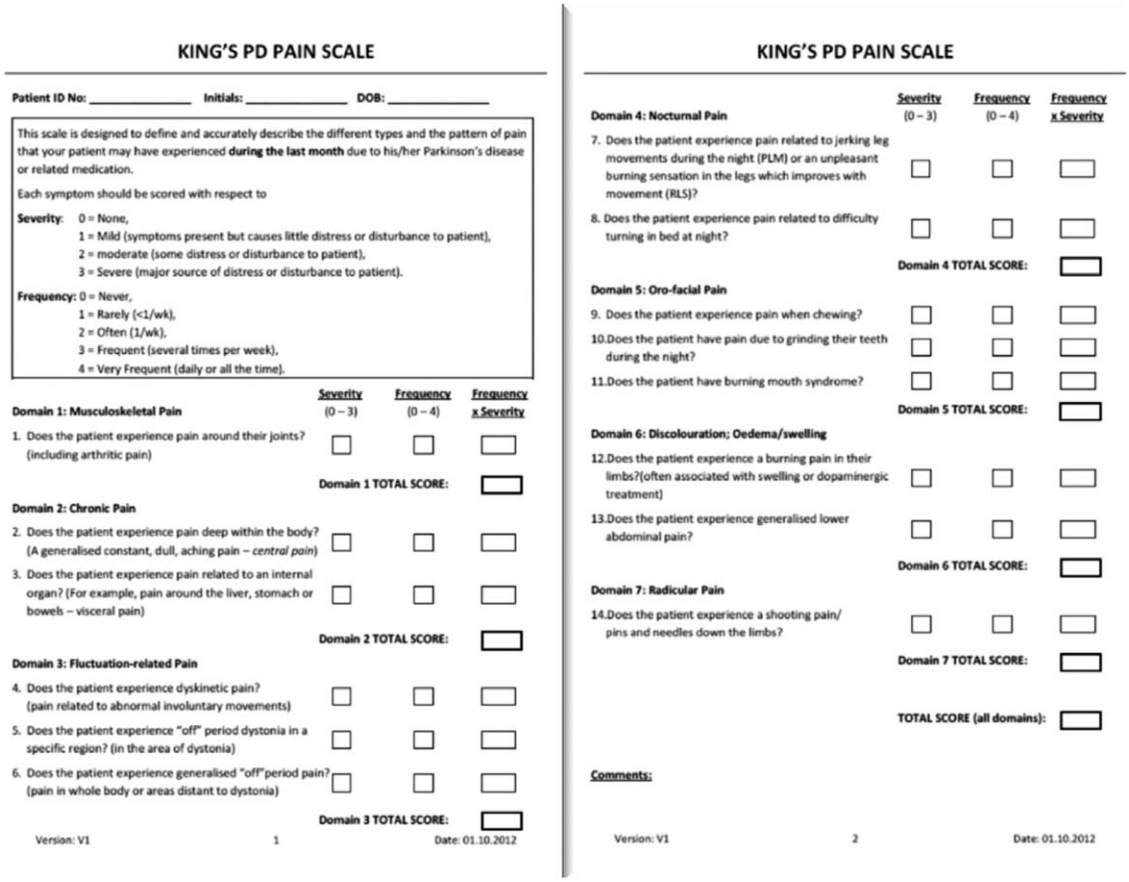
The KPPS has seven domains including 14 items. Domains 1 (musculoskeletal pain) and 2 (chronic pain) are nociceptive pain; neuropathic pain is included in domains 2 and 6 (discoloration; edema/swelling). Additionally, the scale includes fluctuation-related pain (domain 3), nocturnal pain (such as pain related to restless legs syndrome) (domain 4), orofacial pain (domain 5), and radicular pain (domain 7). 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 subscore of 0 to12, the sum of which gives the total score with a theoretical range from 0 to 168. This pattern has been successfully used in various widely validated scales.[8]

In addition to taking medical history and completing the KPPS, the following assessments, validated for PD, were applied (Table 1):

- Hoehn and Yahr (HY) classification[12]
- Scale for Outcomes in PD-Motor (SCOPA-Motor)[13,14]
- Non-Motor Symptoms Scale (NMSS)[8]
- Clinical Impression of Severity Index in PD[15]
- Hospital Anxiety Depression Rating Scale (HADS)[16]
- EQ-5D-3L, a generic, preference-based health-related quality of life measure[17]
- PDQ-8, a specific instrument for assessment of health-related quality of life in PD[18]
- Parkinson's disease sleep scale-version 2 (PDSS-2)[19]
- Wearing-Off Questionnare 9 (WOQ-9), recommended for screening of WO in PD[20]
- Visual analog scales (VAS) for pain severity and frequency[21]

Procedure

Patients were recruited from the Parkinson's clinic at the center of excellence at King's and seven UK



KING'S PD PAIN SCALE

Patient ID No: _____ Initials: _____ DOB: _____

This scale is designed to define and accurately describe the different types and the pattern of pain that your patient may have experienced **during the last month** due to his/her Parkinson's disease or related medication.

Each symptom should be scored with respect to

Severity: 0 = None,
1 = Mild (symptoms present but causes little distress or disturbance to patient),
2 = moderate (some distress or disturbance to patient),
3 = Severe (major source of distress or disturbance to patient).

Frequency: 0 = Never,
1 = Rarely (<1/wk),
2 = Often (1/wk),
3 = Frequent (several times per week),
4 = Very Frequent (daily or all the time).

	Severity (0 – 3)	Frequency (0 – 4)	Frequency x Severity
Domain 1: Musculoskeletal Pain			
1. Does the patient experience pain around their joints? (including arthritic pain)	☐	☐	☐
Domain 1 TOTAL SCORE:			☐
Domain 2: Chronic Pain			
2. Does the patient experience pain deep within the body? (A generalised constant, dull, aching pain – *central pain*)	☐	☐	☐
3. Does the patient experience pain related to an internal organ? (For example, pain around the liver, stomach or bowels – visceral pain)	☐	☐	☐
Domain 2 TOTAL SCORE:			☐
Domain 3: Fluctuation-related Pain			
4. Does the patient experience dyskinetic pain? (pain related to abnormal involuntary movements)	☐	☐	☐
5. Does the patient experience "off" period dystonia in a specific region? (in the area of dystonia)	☐	☐	☐
6. Does the patient experience generalised "off"period pain? (pain in whole body or areas distant to dystonia)	☐	☐	☐
Domain 3 TOTAL SCORE:			☐

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KING'S PD PAIN SCALE

	Severity (0 – 3)	Frequency (0 – 4)	Frequency x Severity
Domain 4: Nocturnal Pain			
7. Does the patient experience pain related to jerking leg movements during the night (PLM) or an unpleasant burning sensation in the legs which improves with movement (RLS)?	☐	☐	☐
8. Does the patient experience pain related to difficulty turning in bed at night?	☐	☐	☐
Domain 4 TOTAL SCORE:			☐
Domain 5: Oro-facial Pain			
9. Does the patient experience pain when chewing?	☐	☐	☐
10. Does the patient have pain due to grinding their teeth during the night?	☐	☐	☐
11. Does the patient have burning mouth syndrome?	☐	☐	☐
Domain 5 TOTAL SCORE:			☐
Domain 6: Discolouration; Oedema/swelling			
12. Does the patient experience a burning pain in their limbs?(often associated with swelling or dopaminergic treatment)	☐	☐	☐
13. Does the patient experience generalised lower abdominal pain?	☐	☐	☐
Domain 6 TOTAL SCORE:			☐
Domain 7: Radicular Pain			
14. Does the patient experience a shooting pain/ pins and needles down the limbs?	☐	☐	☐
Domain 7 TOTAL SCORE:			☐
TOTAL SCORE (all domains):			☐

Comments:

Version: V1 2 Date: 01.10.2012

FIG. 1. The King's Parkinson's Disease Pain Scale (KPPS).

centers, and the IPMDS non-motor PD study group network centers in Sweden, Germany, Italy, and Romania. As in NMSS validation studies, the scales were administered in English.[8]

Consecutive patients with a confirmed diagnosis of PD (UK PD Brain Bank criteria[22]) were administered the NMSQuest, and those answering "yes" to question 10 (unexplained pain) were consented and recruited. Patients were assessed in "on" state.

Interobserver reliability was assessed by simultaneous and independent evaluation by two raters. Test–retest reliability was evaluated at baseline and at follow-up assessment 7 to 15 d later by the same rater in stable patients (controlled by both pain VAS = baseline ± 5%).

Non-spousal, non-PD controls were also recruited from outpatient clinics and matched by age and sex. Control subjects underwent HADS, EQ-5D-3L, and KPPS without the dyskinesia and motor fluctuations section.

Ethical Aspects

All participants provided informed consent. The study was approved by the respective hospital ethical committees/institutional review boards. In the United Kingdom, the study was adopted by the UK national CRN (UKCRN No 13344).

Data Analysis

Data from individual centers were collected centrally, entered in a web-based anonymized database (National Institute of Health Research, Biomedical Research Centre), and transferred to the Neuroepidemiology Unit at Carlos III Institute of Health, Madrid (Spain), for analysis.

In addition to descriptive statistics to define the sample, the following clinimetric attributes were assessed:

1. *Acceptability:* A 95% value of computable data was considered acceptable.[23] Fifteen percent was accepted as maximum value for floor and ceiling effect.[24] Mean and median difference was considered acceptable at less than 10% of maximum observed value. Limits for skewness were −1 and +1.[25] Acceptability was analyzed separately for patients and controls. Other items were determined for patients only (target population).
2. *Internal consistency*: Cronbach's α coefficient, corrected item the total correlation, and item homogeneity were determined. Criterion values were 0.70[26] or higher, greater than 0.20,[27] and greater than 0.20 (for a broad construct),[28] respectively.
3. *Dimensionality*: an exploratory factor analysis by principal component factor method, with

TABLE 1. Scales used in the study

Name of Scale	Scale Characteristics	Patients		Controls
		Rater-Based	Patient-Based	
Hoehn & Yahr staging	Motor staging of PD: Original staging: 1, 2, 3, 5, and 5.	X		
SCOPA-Motor scale	Assessment of motor disability and complications Ítem score: 0 (normal) to 3 (severe) Total score: sum of ítems (0-75)	X		
Non-Motor Symptoms Scale (NMSS)	Assessment of NMS over the last month: 30 items in 9 domains. Item score: severity (0-3) multiplied by frequency (1-4). Total score: sum of domains (0-360)	X		
Clinical Impression of Severity Index (CISI-PD)	Clinical estimate of current PD global severity Item score: 0 (normal) to 6 (very severe) Total score: sum of ítems (0-24).	X		
King's PD Pain Scale (KPP)	Assessing pain over the last month 14 items in 9 domains (see Fig. 1) Item score: severity (0-3) multiplied by frequency (0-4). Total score: sum of domains (0-168)	X		X
Hospital Anxiety and Depression Scale (HADS)	Assessing current description of feelings 14 items, 7 for anxiety and 7 for depression Item score: 0 (best case) to 3 (worst case) Total score: sum of ítems (0-42)		X	X
European Quality of Life-5 Dimensions-3 Levels (EQ-5D-3L)	5 items for assessment of health state today Item score: 1 (best case) to 3 (worst case) Total score: sum of ítems (5-15)		X	X
Parkinson's Disease Questionnaire - 8 items (PDQ-8)	Assessment of HRQoL over the last month 8 items, each scoring 0 to 4 Total score: sum of ítems (0-32). PDQ-8 Summary Index: % total score of maximum possible score		X	
Parkinson's Disease Sleep Scale 2 (PDSS-2)	15 items assessing sleep in the last week Item score: 0 (best case) to 4 (worst case) Total score: sum of ítems (0-60)		X	
Wearing-Off Questionnaire - 9 items (WOQ-9)	9 items assessing wearing off in the past month for presence and improvement of symptom (yes/no) Item score: 1 for "yes" or 0 for "no" Total score: sum of ítems (0-9)		X	
Visual analogue pain scales	Assessing pain over the last month Severity (0, not at all to 100, very severe) Frequency (0, not at all to 100, all the time) Total score: severity multiplied by frequency (0-10,000)		X	

orthogonal rotation, was completed. Kaiser-Mayer-Olkin measure of sampling adequacy and Bartlett's sphericity test were applied, and values greater than 0.6 and $P < 0.05$, respectively, were considered adequate.[29]

4. *Hypotheses testing*: An a priori hypothesis was made that KPPS scores would show close correlation ($r_s > 0.50$)[30] with visual analog pain scales and item 27 of the NMSS (convergent validity). Moderate ($r_s = 0.35$-0.50) or high correlations were also expected with the corresponding items/domains of SCOPA motor, WOQ-19, and PDSS-2. Correlation between KPPS domains (internal validity) was expected to be low or moderate, given the diversity of pain modalities. The known groups validity (sex, HY-based severity levels,

TABLE 2. Demographics of patients and controls

Item	Patients	Controls
Number	178	83
Male sex[a]	122 (62.92%)	51 (61.45%)
Age[b]	64.38 ± 11.38: 29-85	64.25 ± 11.10
Education[b]	14.05 ± 3.80: 9-24	14.64 ± 4.25
Duration of disease[b]	5.40 ± 4.93: 0-26	N/A
HY stage 1[a]	38 (21.35%)	N/A
HY stage 2[a]	85 (47.75%)	N/A
HY stage 3[a]	42 (23.60%)	N/A
HY stage 4[a]	12 (6.74%)	N/A
HY stage 5[a]	1 (0.56%)	N/A
Levodopa equivalent daily dose	539.49 ± 435.77 mg	N/A

[a]Shown as number (%).
[b]Shown as mean ± SD (years): range.

TABLE 3. Descriptive statistics of the assessments in the study

	Mean	SD	Range
Patients			
SCOPA-Motor Scale	17.38	10.28	1-65
Non-Motor Symptoms Scale	60.71	44.31	0-235
Clinical Impression of Severity Index	6.54	3.93	0-19
Hospital Anxiety and Depression Scale: Anxiety	6.17	4.56	0-20
Hospital Anxiety and Depression Scale: Depression[a]	5.44	3.96	0-18
EQ-5D-3L[a]	0.52	0.28	−0.43-1
PDQ-8	27.84	20.28	0-93.75
Parkinson's Disease Sleep Scale-2	18.25	11.20	0-51
WOQ-9—Total of fluctuating symptoms	3.15	2.62	0-9
Visual analogue pain scale—Frequency	55.57	25.27	0-100
Visual analogue pain scale—Severity	53.85	23.27	0-100
Controls			
Hospital Anxiety and Depression Scale: Anxiety	5.37	3.72	0-16
Hospital Anxiety and Depression Scale: Depression[a]	3.06	2.85	0-14
EQ-5D-3L[a]	0.77	0.23	−0.18-1

[a]Difference between patients and controls was significant ($P < 0.0001$).

EQ-5D-3L Pain categories) was explored with the Mann-Whitney or Kruskal–Wallis test.

5. *Precision* of the scale was determined by means of the standard error of measurement (SEM) on the test–retest reliability,[26] considering satisfactory an SEM of less than one-third standard deviation at baseline.[24]
6. *Reliability*: For both test–retest (n = 47 patients) and inter-observer reliability (n = 49), item scores reproducibility was tested with weighted kappa index with square weights and total scores with intraclass correlation coefficient. Values higher than 0.70 were deemed acceptable.[26,31]

For comparison between patients and controls, the Mann-Whitney test was used and corrected by Benjamini-Hochberg method for multiple comparisons.[32] Based on the medical history, levodopa-equivalent daily dose was calculated according to Tomlinson et al.[33]

Results

One hundred seventy-eight PD patients with otherwise unexplained pain and 83 non-spousal non-PD controls, matched by age, sex, and duration of education, were studied. Demographics are shown in Table 2; scores of applied measures in Table 3.

Differences between patients and controls for HADS-Depression and EQ-5D-3L were significant ($P < 0.0001$), but not for HADS-Anxiety. The KPPS data for both groups are shown in Table 4. Although scores, as a whole, were higher (worse) in PD patients, only items 1, 5, 6, 8, and 14 reached statistical significance between groups after correction. The KPPS

TABLE 4. Scores of the King's Parkinson's Disease Pain Scale

	Patients			Controls		
Items	Mean	SD	Range	Mean	SD	Range
1. Pain around joints (musculoskeletal)[a]	6.02	4.07	0-12	3.66	3.69	0-12
2. Pain deep within the body	2.13	3.76	0-12	0.83	2.24	0-12
3. Pain related to internal organ	1.24	2.82	0-12	0.54	1.73	0-9
4. Dyskinetic pain	1.24	3.05	0-12	0.25	1.29	0-8
5. "Off" dystonia in a region[a]	2.42	3.90	0-12	0.18	0.83	0-6
6. Generalized "off" period pain[a]	1.62	3.33	0-12	0.19	1.09	0-9
7. PLM or RLS-associated pain	1.60	3.08	0-12	0.61	1.85	0-9
8. Pain while turning in bed[a]	3.32	4.08	0-12	0.88	2.16	0-9
9. Pain when chewing	0.37	1.47	0-8	0.05	0.44	0-4
10. Pain due to grinding teeth	0.34	1.58	0-12	0.05	0.35	0-3
11. Burning mouth syndrome	0.26	1.29	0-12	0.14	1.32	0-12
12. Burning pain in the limbs	1.35	3.08	0-12	0.46	1.72	0-9
13. Lower abdominal pain	0.94	2.44	0-12	0.41	1.79	0-12
14. Shooting pain/pins & needles[a]	2.36	3.53	0-12	1.07	2.49	0-12
Domains						
1. Musculoskeletal pain[a]	6.02	4.07	0-12	3.66	3.69	0-12
2. Chronic pain[a]	3.37	5.53	0-24	1.37	3.23	0-18
3. Fluctuation-related pain[a]	5.27	8.26	0-36	0.63	2.30	0-14
4. Nocturnal pain[a]	4.91	5.87	0-24	1.49	3.36	0-15
5. Oro-facial pain[a]	0.97	3.00	0-22	0.24	1.42	0-12
6. Discoloration, edema/swelling[a]	2.29	4.49	0-24	0.87	2.66	0-15
7. Radicular pain[a]	2.36	3.53	0-12	1.07	2.49	0-12
Total score[a]	25.19	22.14	0-102	9.34	12.58	0-63

[a]Significant difference between patients and controls after Benjamini-Hochberg correction for multiple comparisons ($P < 0.026$).

TABLE 5a. Convergent validity of the King's Parkinson's Disease Pain Scale

Domains	VAS Total	NMSS Item 27	PDQ-8 Item 8	PDSS-2 Item 10	PDSS-2 Item 11	PDSS-2 Item 12
1. Musculoskeletal pain	0.45	0.22	0.16	0.24	0.19	0.22
2. Chronic pain	0.34	−0.04*	0.17	0.27	0.25	0.34
3. Fluctuation-related pain	0.24	0.08*	0.41	0.38	0.36	0.39
4. Nocturnal pain	0.32	0.10*	0.36	0.44	0.36	0.47
5. Oro-facial pain	0.21	−0.08*	0.09*	0.22	0.17	0.29
6. Discoloration, edema/swelling	0.24	−0.07*	0.25	0.34	0.38	0.37
7. Radicular pain	0.23	−0.04*	0.26	0.32	0.32	0.37
Total score	0.55	0.21	0.45	0.50	0.47	0.58

*Nonsignificant Spearman rank correlation coefficients. All others, $P < 0.05$ or lower.
VAS, visual analog scale; NMSS, non-motor symptom scale; PDQ-8, Parkinson's disease questionnaire - 8 items; PDSS-2, Parkinson's disease sleep scale—version 2.

domains and total score, however, were significantly higher in patients, although the difference in orofacial pain domain did not reach statistical significance.

No data were missing in the KPPS. Floor effect was observed in all domains, from 44.38% (nocturnal pain) to 84.83% (oro-facial pain), with exception of musculoskeletal pain (15.17%). A higher floor effect was found for all domains in the control group. No ceiling effect was noted for any domain in any group, except a marginal one for item 1 in the patient group. The KPPS total score showed negligible floor or ceiling effects (both, 0.56%) in patients, whereas a marginal floor effect (19.28%) was present in controls. The difference between mean and median KPPS total score was less than 10% of the maximum observed value, and skewness was marginally high (1.48 for patients).

Factor analysis identified four factors in the KPPS explaining 57% of the variance (Kaiser-Mayer-Olkin, 0.73; sphericity test, $P < 0.001$). Factor 1,"Internal pains", included chronic pain, generalized abdominal pain, and pain down the limbs items (items 2, 3, 13, and 14); factor 2 was coincident with the domain "fluctuation-related pain" (items 4-6); factor 3, "pain in limbs", included item 1 (musculoskeletal pain), items 7 and 8 (domain "nocturnal pain"), and 12 (burning limb pain); factor 4 overlapped with "oro-facial pain" of the KPPS.

Cronbach's alpha was 0.78, with deletion of any item barely modifying this value (0.75-0.79). Item-total correlation mean value was 0.40, ranging from 0.17 (pain when chewing) to 0.54 (generalized "off" period pain). Item homogeneity was 0.22.

Correlation coefficients of the KPPS domains and total score with other pain measures are shown in Table 5a. Correlations were high, with VAS total score ($r_S = 0.55$) and item 12 of the PDSS-2 (painful posturing in early morning; $r_S = 0.58$). Other correlations were weak or moderate. We found a high correlation between PDSS-2 item 4 and KPPS item 7 ($r_S = 0.54$), both related to restless legs syndrome, and between PDSS-2 item 9 and KPPS item 8 ($r_S = 0.52$) related to difficulty turning in bed. The KPPS Item 4 (dyskinetic pain) showed a high correlation ($r_S = 0.64$) with the dyskinesia score of SCOPA-Motor (items 18 and 19). The KPPS items 4, 5, and 6 (pain in "off" periods) reached a moderate/high association ($r_S = 0.43$-0.44) with the fluctuations score of SCOPA-Motor (items 20 and 21). Finally, a moderate correlation ($r_S = 0.47$) was found between KPPS total score and number of fluctuating symptoms in the WOQ-9 and between items 5 and 6 of the KPPS (pain in "off" periods) and the number of fluctuating symptoms in the WOQ-9 ($r_S = 0.46$).

The correlation of the KPPS total score with other variables in the study is shown in Table 5b. The KPPS total score was not significantly different between sexes but significantly increased with increasing HY

TABLE 5b. Correlation of the King's Parkinson's Disease Pain Scale with other variables in the study

	Spearman *R*	*P*
Age	0.00	1.00
Years of education	−0.19	0.01
Age at onset of PD	−0.14	0.07
PD duration	0.36	<0.0001
Hoehn and Yahr staging	0.24	0.001
SCOPA-Motor Examination	0.27	0.0003
SCOPA-Motor ADL[a]	0.58	<0.0001
SCOPA-Motor Complications	0.49	<0.0001
SCOPA-Motor Total score[a]	0.51	<0.0001
Non-Motors Symptoms Scale[a]	0.59	<0.0001
HADS-Anxiety	0.43	<0.0001
HADS-Depression	0.48	<0.0001
CISI-PD Total score[a]	0.53	<0.0001
LEDD	0.30	<0.0001
EQ-5D-3L Summary Index[a]	−0.56	<0.0001
PDQ-8 Summary Index[a]	0.58	<0.0001

[a]High correlation with King's Parkinson's Disease Pain Scale total score.
PD, Parkinson's disease; SCOPA, Scale for Outcomes in PD; HADS, Hospital Anxiety Depression Rating Scale; CISI-PD, Clinical Impression of Severity Index in PD; LEDD, levodopa-equivalent daily dose; EQ-5D-3L, European quality of life-5 dimensions-3 levels; PDQ-8, PD Questionnaire-8 items.

stage ($P = 0.003$) and EQ-5D-3L item (pain/discomfort level) ($P < 0.0001$).

The KPPS total score inter-rater reliability analysis found an intraclass correlation coefficient (two-way, random effect) = 0.99, and the test–retest (interval between evaluations: 13.79 ± 5.65 d; one-way, random effect) = 0.96.

For both reliability analyses, weighted kappa for items ranged from 0.76 to 1.00, most of the results being 0.90 or higher. The SEM of the KPPS total score was 4.92 (1/3 SD at baseline: 8.21).

Discussion

We report the development of the first scale for a global and bedside evaluation of the burden and characterization of various phenotypes of pain in PD patients. The scale is easy to administer, requiring the investigator to ask the patient 14 questions and to score both severity and frequency within approximately 10 to 15 minutes. Data from seven domains provide information on different types of pain in PD, broadly classified to nociceptive and neuropathic patterns. Specifically, KPPS captures pain ranging from wearing off related pain to central, orofacial, and radicular pain. A total score provides the overall sum of the burden of pain in PD similar to one obtained in analogous scales such as PDSS-2 and NMSS.[8,19] Despite the complex construct, the scale is valid and reliable. Importantly, a high correlation exists between KPPS score and severity of disease as well as health-related quality of life (HrQol) in PD.

As usual in clinical samples, intermediate stages of PD were overrepresented, although we included patients in all stages. Importantly, the patient population studied ranged from those "just diagnosed" to 45 years disease duration, making this a representative sample of PD population. As such, we believe that the applicability of the scale should be generalizable to the broad range of patients except those with the most severe cognitive impairment, where the scale could not be tested. Patients were tested in "on" state as recommended by the IPMDS. This is also reflected in the fact that 65% of the population studied had motor fluctuations (as per WOQ-9 scale assessment), thus increasing the likelihood of report of fluctuation-related pain.

Management of pain in PD is complicated by the fact that there are as yet no standardized tools for a global assessment of pain in PD, taking into account the various types of pain as well as distinction, as far as possible, between pain directly related to the pathogenic process of PD and pain that arises secondary to comorbidity of PD.[5]

Regarding clinimetric quality, quality of data obtained in this study was very satisfactory with no missing data. Acceptability parameters of the domains showed the floor effect of diverse magnitude, as a whole, but no ceiling effect, whereas the total score was free of both effects. The floor effect of the domains was a consequence of low prevalence of the corresponding types of pain in the sample, clearly reflected through the higher floor effect in the control group. Other acceptability aspects showed satisfactory results. The factorial structure was consistent with a regional distribution of pain (factors 1, 2, and 4) or dependence on fluctuations. This grouping of symptoms was partially coincident with the primary division in domains of the scale and offers an additional option for data analysis.

Considering the primary structure in domains of the scale (five with one or two items) and its partial coincidence with the factor analysis, internal consistency testing showed that the corresponding parameters were satisfactory. Because the domains were heterogeneous and some consisted of one or two items only, internal consistency is reported for the whole scale and not the individual domains.

Data on convergent validity show a satisfactory association with a range of measures related to global pain perception, pain-related manifestation during sleep and fluctuations, a set of aspects very consistent with the conceptual framework embedding pain in PD. High correlations with motor disturbances, total score of the NMS, Clinical Impression of Severity Index in PD, and QoL measures provide additional data favoring the multiple associations that pain can settle with many other aspects of the disease and influence on HrQoL.[34,35] Also, the KPPS total score increased with increasing HY stage and categories of the EQ-5D-3L item pain/discomfort, showing a satisfactory discriminative validity. The scale did not show significant sex differences, a finding contrary to other reports.[36,37]

Finally, both aspects of reliability, inter-rater and test–retest, were excellent for items and domains. Because of the strong relationship between the SEM and reliability, the precision of the scale was very satisfactory. The quality of these properties predict an adequate responsiveness for long-term longitudinal observations and clinical trials.[38,39]

The study allows discussion regarding frequency of occurrence and localization of the different types of pain as detailed in the KPPS compared with an age-matched control group. Despite excluding patients with a clear "pain-related condition" (eg, significant osteoarthritis), item 1 of the scale (musculoskeletal pain) showed a significantly high mean value. This is, however, not surprising because musculoskeletal pain is highly prevalent in PD and may not necessarily imply arthritis.[11] The higher rate of musculoskeletal pain in PD than controls suggests that such pain

occurs in PD regardless of duration or severity of disease. Other significantly frequent pain in PD (compared with controls) included "off related pain," "pain while turning in bed," as well as "shooting pain" and "pins and needles". "Off"-related pain indicates pain of motor fluctuations and is expected to be present in the levodopa-treated cohort within the patients tested with KPPS. Nighttime pain, while turning in bed, is possibly reflective of nocturnal akinesia, a common problem in PD. Finally, shooting pain and pins and needles represent radicular pain and could be linked to indirectly aggravated pain or pain arising from arthritis or joint-related problems.

Limitation of the Current Study

The KPPS is an evaluative measure for pain-related symptoms in PD with "lumping" of various types of pain symptoms together. However, this allows addressing the overall burden of pain-related symptoms in an individual patient and also may allow identification of the subtype of pain, which may be relevant in a patient. We excluded patients with clinically relevant dementia for whom report of subjective aspects of pain would be unreliable or impossible.

In conclusion, we present validation data for the first PD-specific pain scale, the KPPS, based on an international multicenter study. Despite the complexity of the structure of the scale, this controlled study provides evidence that the KPPS is a valid and reliable scale. Further large-scale linguistic validation studies are now needed. ■

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