Perceived Physical Activity Decline as a Mediator in the Relationship Between Pain Catastrophizing, Disability, and Quality of Life in Patients with Painful Diabetic Neuropathy

ORIGINAL ARTICLE

Perceived Physical Activity Decline as a Mediator in the Relationship Between Pain Catastrophizing, Disability, and Quality of Life in Patients with Painful Diabetic Neuropathy

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■ **Abstract**

Background: To fully understand the burden of painful diabetic neuropathy (PDN), we investigated the relationship of pain catastrophizing with disability and quality of life in patients with PDN. Furthermore, we studied the mediating roles of physical activity and/or decline in physical activity.

Methods: This questionnaire-based cross-sectional study included 154 patients with PDN. Linear regression analyses, adjusted for age, gender, pain intensity, and insulin treatment, were performed to assess the association of pain catastrophizing (Pain Catastrophizing Scale [PCS]) with the outcome variables disability (Pain Disability Index [PDI]) and quality of life (Norfolk Quality of Life Questionnaire Diabetic Neuropathy Version [QOL-DN]). The mediating roles of actual physical activity (Physical Activity Rating Scale [PARS]) and perceived Physical Activity Decline (PAD) were assessed using mediation analyses according to Baron and Kenny.

Results: This study included 154 patients (62% male). Mean age was 65.7 years (SD = 6.6). PCS (M = 20.3, SD = 13.1) was significantly associated with PDI (M = 32.4, SD = 17.0; R^2 = 0.356, $P < 0.001$), QOL-DN (M = 52.6, SD = 26.1; R^2 = 0.437, $P < 0.001$), and PAD (M = 7.4, SD = 5.7; R^2 = 0.087, P = 0.045). PAD acted as a partial mediator in the associations of PCS with PDI and QOL-DN, respectively. There was no association of PCS with PARS.

Conclusions: Pain catastrophizing was associated with increased disability and decreased quality of life in patients with PDN. Also, it was associated with a perceived decline in physical activity, which had a mediating role in the association between catastrophizing and disability and quality of life, respectively. This study emphasizes the role of catastrophic thinking about pain and the experienced loss in daily activities due to PDN. ■

Key Words: painful diabetic neuropathy, chronic pain, neuralgia, diabetic, psychology, polyneuropathy

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INTRODUCTION

Up to 20-60% of patients with diabetes mellitus develop painful diabetic neuropathy (PDN).[1] PDN is known to have a negative impact on physical and mental quality of

life (QOL) and is associated with socioeconomic consequences including loss of work time.[2] Sensory and motor deficits in patients with PDN can lead to less engagement in physical activity, which, in turn, can further impair psychosocial well-being.[3,4] Research has shown that patients with PDN often suffer from enhanced levels of anxiety, fears, and depression.[5]

The interpretation of pain and its consequences on daily life are influenced by behavioral and cognitive efforts used in the attempt of dealing with pain. An example of a coping strategy that has received much attention in studies with patients with various chronic pain syndromes is pain catastrophizing.[6–10] Pain catastrophizing is defined as a negative cognitive set brought to bear during actual or anticipated pain experience, as it refers to the process during which pain is interpreted as being extremely threatening.[8] It has been suggested that as a function of negative experiences involving pain, catastrophic thinking may lead to the development of a coping style that leads patients to be excessively vigilant to pain-related stimuli, to focus excessively on pain sensations, and to expect that aversive stimuli will result in experiences of heightened pain.[11] Pain catastrophizing, as measured with the Pain Catastrophizing Scale (PCS)[12], has been associated with heightened pain experience in patients with different types of neuropathic pain such as postherpetic neuralgia[6], phantom limb pain,[7] and pain associated with spinal cord injury.[10] It has also shown to have a negative impact on the level of disability, depression, and anxiety and increase consumption of analgesic medication and pain-related behavior.[10,11,13]

An association of pain catastrophizing with decreased physical activity has been found in groups of patients with whiplash and soft-tissue injuries.[14] The association of pain catastrophizing with physical activity, QOL, and perceived disability in patients with PDN has not yet been fully elucidated. It is plausible that catastrophic thinking is also associated with a lower level of physical activity and more perceived disability in patients with PDN. The question arises whether catastrophic thinking leads to an experienced decline in physical activity as compared to patients' habitual activity level, or whether it is associated with the actual level of physical activity. Furthermore, it is unknown whether the level of physical activity affects perceived disability and/or QOL in patients with PDN. The aim of this study, therefore, was to further unravel the underlying mechanisms linking pain catastrophizing to (perceived) physical activity, disability, and QOL in patients with PDN. We hypothesized that pain catastrophizing is associated with perceived disability and decreased QOL in patients with PDN and that these associations are mediated by the experienced decline in physical activity rather than the actual level of physical activity.

METHODS

Patients

In this study, 154 patients with type 2 diabetes mellitus, aged > 18 years who suffered from peripheral polyneuropathy, were included. Eligibility for this study was based on the following: providing written informed consent, having type 2 diabetes mellitus, aged > 18 years, and suffering from peripheral polyneuropathy. Additionally, the Diabetic Neuropathy Symptom Score (DNS)[15] was used to diagnose diabetic neuropathy. This scale consists of 4 items: (1) unsteadiness in walking; (2) pain; (3) burning or aching at legs or feet, prickling sensations in legs or feet; and (4) numbness in legs or feet.[15] The DNS has been validated for diabetic polyneuropathy and has shown to have a high sensitivity and specificity.[15] Neuropathic pain in the feet was assessed using the interview section of the Douleur Neuropathique 4 Questions (DN4-interview), which consists of seven items relating to the pain description (burning, painful cold, electric shocks) and to its abnormal sensations (tingling, pins and needles, numbness, itching).[16] DN4 and DN4-interview scores showed a high diagnostic accuracy for painful diabetic polyneuropathy.[16] Patients with a DNS score $\geq$1 and neuropathic pain in the feet (DN4 $\geq$ 4) for at least 3 months and being clinically stable were included. Patients were excluded if there were other conditions that could lead to pain in the feet and/or damage to the peripheral nervous system and if they were not able to understand the Dutch language.

Procedure

Letters of interest were sent to patients derived from a database of patients with type 2 diabetes from a regional hospital in the south of the Netherlands (VieCuri, Venlo, the Netherlands). In total, a number of 2142 letters of interest were sent to patients randomly selected from the database. A total of 388 letters of interest were returned, of which 237 (61%) patients indicated that they were willing to participate in the study. Of the 151 patients who declined to participate, 94 patients reported the reason: no neuropathic pain (n = 54), type I DM (n = 23), death (n = 9), personal circumstances (n = 4), moved to a different address (n = 2), phantom

limb pain (n = 1), no DM (n = 1). Of the 237 patients who received a questionnaire, 183 actually filled in and returned the questionnaire (47% of 388 patients that returned the letter of interest). Inclusion criteria were independently checked by a research assistant and a physician in rehabilitation medicine. Of the 183 patients, 154 met the criteria for inclusion. Informed consent was obtained from all subjects; the experimental protocol was approved by the Medical Ethics Committee of Maastricht University, the Netherlands. The procedure of inclusion is shown in Figure 1.

Measures

All data were retrieved by self-report questionnaires. Patient characteristics included sociodemographic factors and pain-related measures. Behavioral factors were measured using various questionnaires, as is described in the following paragraphs.

Patient Characteristics. The following factors were assessed: age (years), gender, nationality, and having insulin treatment for DM (yes/no).

Pain and Pain Catastrophizing. Duration of complaints of neuropathic pain was assessed (months). In addition, pain intensity was measured using a visual analog scale (VAS), ranging from 0 to 10. Pain catastrophizing was measured using the Dutch version of the validated 13-item PCS. This questionnaire measures negative thoughts and beliefs during actual or anticipated painful experiences. The items are scored on a 5-point Likert scale with scoring possibilities ranging from "not at all" (score = 0) to "always" (score = 4). The PCS total score is computed by summing responses to all 13 items and ranges from 0 to 52. High scores indicate that more catastrophic thoughts or feelings are experienced. Psychometric properties of the PCS appeared adequate in previous research: It correlated highly (r = 0.73) with the catastrophizing subscale of the Dutch Pain Cognition List (PCL) and had a good temporal stability (Pearson's r^2 = 0.92).[17] The PCS has shown to have adequate to excellent internal consistency.[18]

Disability. Perceived disability was measured using the Pain Disability Index (PDI). This 7-item questionnaire investigates the magnitude of the self-reported disability in different situations such as work, leisure time, activities of daily living (ADLs), and sports. Each item is scored on a numeric rating scale ranging from 0 (no perceived disability) to 10 (maximum perceived disability). Scores of the individual items were added up to provide the total score. PDI has shown to be internally reliable (Cronbach's alpha = 0.86) and significantly correlated with objective indices of disability such as time spent in bed, psychosomatic symptoms, stopping activities because of pain, work status, pain duration, usual pain intensity, QOL, pain extent, and education (r = 0.74).[19]

Quality of Life. Quality of life was measured using the 47-item Norfolk Quality of Life Questionnaire, Diabetic Neuropathy Version, QOL-DN[20], a self-administered questionnaire designed to capture and quantify the perceived impact of diabetic neuropathy on the QOL, physical, and psychosocial functioning of patients with

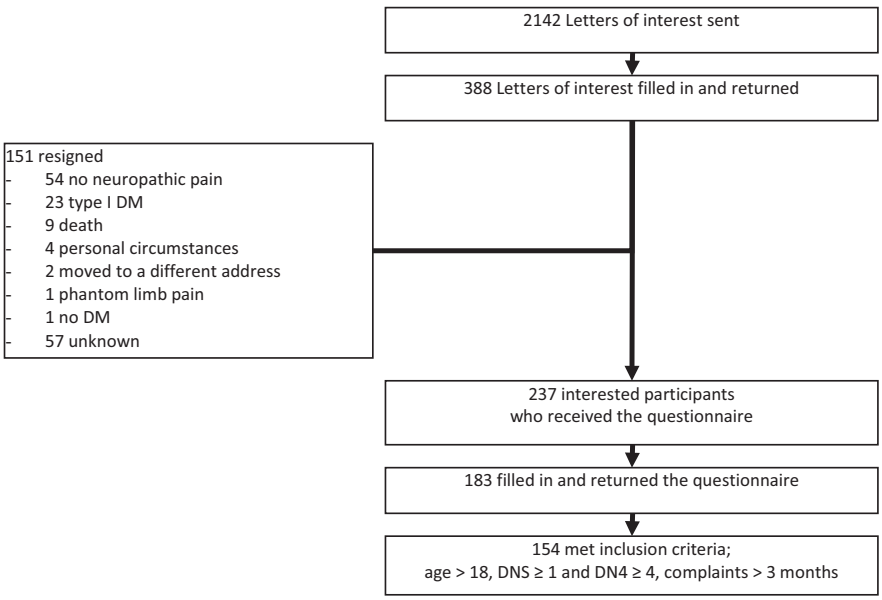

Figure 1. Flowchart of inclusion procedure.

diabetic neuropathy. Fourteen of the items are of a health-related, biographical nature and are not scored. Therefore, they were excluded from this study. Items 1–7 (Part I) are an inventory of symptoms of neuropathy in the feet, legs, arms, and hands, respectively. For each body part separately, the presence of a symptom is scored as 1 and absence of a symptom is scored as 0. The absence of the symptom in all body parts is checked as "none." Items 8-35 (Part II) concern ADLs and are scaled on a 5-point Likert scale ranging from 0 ("not a problem") to 4 ("severe problem"). The 35 scored questions comprise the entire scale and can be grouped according to small fiber, large fiber, and autonomic nerve function symptoms and ADLs. Intraclass correlation coefficients have shown to be > 0.9 for most domains.[20] Internal consistency of the fiber-specific domains using Cronbach's alpha was considered > 0.6 and up to 0.8.[20] Scores in individual domains (Parts I and II) were aggregated to provide a total score.

Physical Activity and Perceived Activity Decline. The level of activity was determined using two concepts: physical activity and perceived activity decline (PAD). Physical activity was measured using the Physical Activity Rating Scale (PARS)[21], which consists of 20 daily activities. On a 5-point Likert scale (range 0–4), patients score how often they have performed these activities in the past 2 weeks. To estimate the pain-related decline in activities, the PAD question was added to the PARS. For each activity, patients were asked to indicate how frequently they had performed the specified activity in the last 2 weeks using the following response categories: never, rarely, now and then, often, and very often. Furthermore, patients indicated whether they would have performed this specific activity more often if they would not have pain. If the answer was yes for a specific item, 1 point was counted. On the contrary, if the answer was no, the score on that item was 0. The total sum score for 20 activities resulted in a score for PAD; a perceived decline in the level of physical activity after the onset of pain as perceived by the patient, with a theoretical range in PAD of 0–20. The internal consistency (Cronbach's alpha = 0.92) and reliability (ICC = 0.93) of PAD have shown to be good.[22]

Statistical Analyses

Data were analyzed using the Statistical Package for Social Sciences for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). Results for groups (baseline characteristics) were expressed as a mean score and standard deviation. Comparisons between two groups were performed using Student's *t*-test for independent samples. To assess the association of pain catastrophizing (PCS) with perceived disability (PDI) and decreased QOL (QOL-DN), linear regression analyses were performed with PDI and QOL-DN as independent variables, adjusted for the study covariates pain intensity, age, gender, and insulin treatment (independent variables).

To evaluate the mediating role of PARS and PAD in the association of pain catastrophizing and perceived disability or QOL, multiple linear regression analyses were performed according to Baron and Kenny.[23] To illustrate this procedure, the analyses for the mediation of PAD in the association of PCS and PDI are described. In the first analysis, PDI was introduced as the dependent variable and PCS, pain intensity, age, gender, and insulin treatment as independent variables (step 1). In the second analysis, PAD was introduced as dependent variable, with the same independent variables as in the first analysis (step 2). The third analysis resemble the first (PDI-dependent variable) with the addition that PAD is added to the earlier set of independent variables (step 3). If PAD acts as mediator in the relation of pain catastrophizing and PDI, the contribution of PCS should be statistically significant in the first and second analyses, whereas the effect should be attenuated in the third analysis after introduction of PAD. To evaluate the mediating role of PARS in the association with PCS and PDI, and the mediating role of both PARS and PAD in the association with PCS and QOL-DN, three identical procedures were performed.

For all multiple linear regression analyses, standardized beta coefficients and their significance were tested under the null hypothesis that the coefficient differed from 0. To control for multicollinearity, variable inflation factors (VIFs) were checked and should all be below three. Data were checked for normality and missing values. Mean imputation was performed to account for missing data in total scores.

RESULTS

Baseline Characteristics And Pain-Related Outcomes

This study included 96 male and 58 female patients with a mean age of 65.7 years (SD = 6.6) (Table 1). Mean duration of complaints of PDN was 72.3 months (SD =

Table 1. Baseline Characteristics

		N	Mean/*n*	SD/%
Demographic variables	Age	154	65.7	± 6.6
	Gender (Male/Female)	154	96/58	62%/38%
	Insulin treatment	154	100	65%
Pain-related measures	Duration of complaints	144	72.3	± 57.6
	Pain intensity	153	4.8	± 2.0
	PCS	151	20.3	± 13.1
Consequences in daily life	QOL-DN	131	52.6	± 26.1
	PDI	150	32.4	± 17.0
	PARS	152	45.3	± 9.0
	PAD	141	7.4	± 5.7

Data are presented as mean ± SD or *n* (%), as appropriate. Age (years), duration of complaints (months), pain intensity (VAS 0-10), PCS, Pain Catastrophizing Scale; QOL, Quality of Life; PDI, Pain Disability Index; PARS, Physical Activity Rating Scale; PAD, Perceived Activity Decline.

57.6), and 65% of the participants were on insulin treatment. Pain-related variables: mean pain intensity score was 4.8 (SD = 2.0), mean PCS score was 20.3 (SD = 13.1), mean PDI score was 32.4 (SD = 17.0), and mean QOL-DN score was 52.6 (SD = 26.1). Activity-related variables: Mean PARS score was 45.3 (SD = 9.0), and mean PAD score was 7.4 (SD = 5.7). There were no differences between men and women on the baseline characteristics or pain-related outcomes ($P > 0.05$ for all variables, Table 1).

Step 1: The Association Between Pain Catastrophizing and Perceived Disability, and QOL, Respectively

PCS significantly contributed to the association with PDI ($\beta = 0.311$, $P < 0.001$) (Table 2). Furthermore, insulin treatment ($\beta = 0.151$, $P = 0.028$) and pain intensity ($\beta = 0.375$, $P < 0.001$) significantly contributed to the association with pain catastrophizing and perceived disability.

PCS was significantly associated with QOL-DN ($\beta = 0.373$, $P < 0.001$) (Table 3), indicating a lower QOL in patients who engage in catastrophic thinking. Also, insulin treatment and pain intensity significantly contributed to the association of pain catastrophizing and quality of life ($\beta = 0.140$, $P = 0.042$ and $\beta = 0.388$, $P < 0.001$, respectively).

Step 2: The Association Between Pain Catastrophizing and Perceived Activity Decline, and Physical Activity, Respectively

PCS was significantly associated with PAD ($\beta = 0.182$, $P = 0.045$), whereas the level of pain intensity showed no contribution to this association ($\beta = 0.151$, $P = 0.095$) (Table 4). There was no statistically significant association of PCS with PARS, indicating that pain catastrophizing seems to be associated with a perceived decline in physical activity rather than with the actual level of physical activity. Only pain intensity showed a statistically significant contribution to the association with pain catastrophizing and physical activity ($\beta = -0.215$, $P = 0.015$) (Table 4).

Table 2. Mediation analyses for Pain Catastrophizing, Perceived Disability, and Physical Activity Decline

	Dependent variable	Independent variable	R^2	Adjusted R^2	Standardized β	*P*-value
1	PDI	PCS	0.356	0.333	0.311	0.000
		Age			0.018	0.791
		Gender			−0.078	0.256
		Insulin treatment			0.151	0.028
		Pain intensity			0.375	0.000
2	PAD	PCS	0.087	0.052	0.182	0.045
		Age			−0.053	0.522
		Gender			0.031	0.711
		Insulin treatment			0.074	0.374
		Pain intensity			0.151	0.095
3	PDI	PCS	0.482	0.457	0.226	0.001
		Age			0.041	0.518
		Gender			−0.082	0.199
		Insulin treatment			0.106	0.100
		Pain intensity			0.307	0.000
		PAD			0.401	0.000

Analyses in three steps to assess mediating role of PAD in the association of PCS and PDI. PDI, Pain Disability Index; PCS, Pain Catastrophizing Scale; PAD, Perceived Activity Decline.

Step 3A: Mediation Analyses of PAD in the Association of Pain Catastrophizing with Perceived Disability

The first and second steps of the mediation analyses are described above. The mediating role of PAD was analyzed in the association of pain catastrophizing and perceived disability. No analyses were performed to investigate the mediating role of PARS, as the obligatory association of PARS with PCS was absent.

The full mediation analysis is shown in Table 2. When introduced as an independent variable, PAD showed to significantly contribute to the association of PCS with PDI ($\beta = 0.401$, $P < 0.001$). The effects of pain catastrophizing, insulin treatment, and pain intensity were all attenuated ($\beta = 0.226$, $P = 0.001$; $\beta = 0.106$, $P < 0.001$; and $\beta = 0.307$, $P = 0.100$, respectively), indicating that Physical Activity Decline acted as a partial mediator in the association between

Table 3. Mediation analyses for Pain Catastrophizing, QOL, and Physical Activity Decline

	Dependent variable	Independent variable	R^2	Adjusted R^2	Standardized β	*P*-value
1	QOL-DN	PCS	0.437	0.414	0.373	0.000
		Age			−0.023	0.738
		Gender			0.047	0.497
		Insulin treatment			0.140	0.042
		Pain intensity			0.388	0.000
2	PAD	PCS	0.087	0.052	0.182	0.045
		Age			−0.053	0.522
		Gender			0.031	0.711
		Insulin treatment			0.074	0.374
		Pain intensity			0.151	0.095
3	QOL-DN	PCS	0.529	0.504	0.319	0.000
		Age			0.012	0.851
		Gender			0.046	0.483
		Insulin treatment			0.091	0.162
		Pain intensity			0.343	0.000
		PAD			0.336	0.000

Analyses in three steps to assess mediating role of PAD in the association of PCS and QOL-DN. QOL-DN, Norfolk Quality of Life Questionnaire -Diabetic Neuropathy Version; PCS, Pain Catastrophizing Scale; PAD, Perceived Activity Decline.

Table 4. Association of Pain Catastrophizing and Physical Activity, and Physical Activity Decline respectively

Dependent Variable	Independent Variable	R^2	Adjusted R^2	Standardized β	*P*-value
PAD	PCS	0.087	0.052	0.182	0.045
	Age			−0.053	0.522
	Gender			0.031	0.711
	Insulin treatment			0.074	0.374
	Pain intensity			0.151	0.095
PARS	PCS	0.097	0.066	−0.131	0.137
	Age			−0.048	0.548
	Gender			0.008	0.325
	Insulin treatment			−0.008	0.317
	Pain intensity			−0.215	0.015

Linear regression analyses of PCS and PARS, and PAD, respectively. PAD, Perceived Activity Decline; PARS, Physical Activity Rating Scale; PCS, Pain Catastrophizing Scale.

pain catastrophizing and perceived disability. VIFs were checked and were all below 3.

Step 3B: Mediation Analyses of PAD in the Association of Pain Catastrophizing with QOL

To assess whether the association of pain catastrophizing and QOL is mediated by Physical Activity Decline, the same set of analyses were performed. PAD showed to significantly contribute to the association with PCS and QOL-DN ($\beta = 0.336$, $P < 0.001$) (Table 3). The effects of pain catastrophizing, insulin treatment, and pain intensity were again all attenuated after the introduction of PAD ($\beta = 0.319$, $P < 0.001$; $\beta = 0.091$, $P = 0.162$; and $\beta = 0.343$, $P < 0.001$, respectively). This analysis shows that Physical Activity Decline also acted as a partial mediator in the association of pain catastrophizing and QOL. VIFs were checked and were all below three.

DISCUSSION

Pain catastrophizing is characterized by a tendency to magnify the threat value of pain stimuli, to feel helpless in the context of pain, and by a relative inability to inhibit pain-related thoughts in anticipation of, during, or following a painful encounter. Mean PCS scores in this sample of Dutch patients suffering from PDN were comparable to scores of patients with other pain syndromes.[6,8,24] We found that pain catastrophizing was associated with increased perceived disability and decreased QOL in patients with PDN. Interestingly, pain catastrophizing was associated with the subjective feeling of loss of physical activities due to pain (perceived Physical Activity Decline), but not the self-reported estimate of one's actual level of activity. Our findings suggest that patients with PDN who catastrophize about their pain experience a greater burden of PDN due to their perceived, but not actual, decline in physical activity.

In the biopsychosocial perspective, pain is considered to be of a complex and multifactorial origin, taking into account biological, psychological, and social factors, resulting in individual differences in motoric, cognitive, and psychophysiological responses.[25] One model within this perspective is the fear-avoidance model, which addresses the way a patient interprets their pain. If pain is interpreted as nonthreatening, patients are likely to stay engaged in daily activities. If, however, patients misinterpret pain as being threatening, a vicious cycle of catastrophic thinking may be initiated leading to excessive fear of pain/injury, resulting in avoidance of physical activities, disuse, depression, and disability.[26,27] The fear-avoidance model has been extensively studied in patients with chronic low back pain[28], but only limited information is available about the way patients with PDN interpret their pain. In line with the fear-avoidance model, this study shows that pain catas-

trophizing can induce the feeling of not being able to be physically active rather than affecting the actual level of physical activity and that this feeling results in perceived disability and a lower QOL in patients with PDN. These results suggest that it is important to address these subjective measures of perceived disability when assessing the effects of chronic pain syndromes on daily life activities and QOL.

It is known that PDN itself has a negative effect on QOL.[1] Our results indicate that catastrophic thinking may play a role in this association. Mean QOL-DN score (52.6) was comparable to other studies in patients with PDN[29]. Studies in patients with various pain conditions have shown that pain catastrophizing negatively influenced depression and anxiety.[10,4] Furthermore, pain catastrophizing has been associated with increased pain-related disability and behavior.[8,30] The mean PDI score in our study (32.4) was comparable to scores of patients with other pain syndromes.[31] To our knowledge, this study is the first study to link catastrophic thinking with QOL and perceived disability in a sample of patients with PDN.

In order to understand the impact of PDN, it is important to differentiate between perceived disability and Physical Activity Decline. Disability refers to problems in executing daily life tasks and activities. Disability has been defined by the World Health Organization as any restriction or lack of ability to perform an activity in the manner or within the range considered normal for a human being.[32] Pain-related disability questionnaires focus on the decrease in capacity in the performance and altered performance of regular activities in the daily life of patients with pain. In contrast, Physical Activity Decline is defined as a decrease in the level of physical activity as perceived by the patient, which is relative to a person's activity level before the onset of the pain.[33] This study shows that patients who engage in catastrophic thinking experience a greater decline in physical activity, while there was no association between catastrophic thinking and the estimated actual level of physical activity. This is in line with previous studies in patients with low back pain.[33,34]

PAD acted as a partial mediator in the associations between catastrophic thinking and perceived disability, and catastrophic thinking and QOL, respectively. This means that catastrophic thinking is not solely a direct predictor for perceived disability and QOL, but that this association is also partially determined by the feeling of loss in physical activity, which, on its turn, leads to increased perceived disability (inability to perform an activity) and lower QOL. Patients who catastrophize about pain, probably also catastrophize about their loss in physical activity, which further strengthens them in feeling disabled and having a lower QOL. The identification of pain catastrophizing as a partial mediator is valuable, as it suggests that an intervention that targets pain catastrophizing will indirectly also improve perceived disability and QOL.

In line with previous studies, pain intensity was a significant contributor in the explanation of the association of pain catastrophizing and perceived disability, QOL and physical activity.[8,35] Pain intensity showed no contribution in the PAD, suggesting that the perception of activity decline is not pain-induced but is probably based on other mechanisms such as pain catastrophizing.

Insulin treatment is known to be highly burdensome due to the method of administration (injections) and the risks of hypoglycemia.[36] Therefore, insulin treatment can be considered a parameter for the severity of diabetes. As expected, insulin treatment was associated with low QOL and perceived disability. Interestingly, insulin treatment showed a lower β-value in its association with QOL and perceived disability as compared to catastrophic thinking, suggesting that the a catastrophic way of thinking is a greater predictor for the experienced burden caused by PDN, than is insulin treatment. The association of insulin treatment and perceived disability was diminished after the addition of PAD to the model, suggesting that insulin treatment seems to result in the feeling of not being able to be as physically active as before, which on its turn causes the perceived inability to perform certain activities. Thus, insulin treatment was not a direct predictor for perceived disability.

This study has several limitations. First, potential participants for this study were derived from an already existing database containing patients with type 2 diabetes. Only 183 of 2142 invited patients filled in and returned the final questionnaire, resulting in a potential self-selection bias. Secondly, diabetes-related information is based on self-report. In order to overcome this issue, we used multiple selected items (DNS ≥ 1 and DN4 ≥ 4) to identify eligible subjects according to our inclusion criteria. In future studies, PDN should be diagnosed by performing a clinical history and peripheral neurological and vascular examination. Thirdly, there was no information available on diabetes-related complications such as retinopathy or nephropathy. Also scores on physical activity were

solely based on self-report and there was no movement registration. It should be noted, however, that information on physical activities in the past can only be obtained based on self-report. Future prospective studies using objective physical measurements are advised, to avoid the influence of a patients' perception or interpretation. For example, accelerometry could be a useful addition to the PARS questionnaire. Lastly, this study has a cross-sectional design in which the dependent and independent variables are simultaneously assessed. For this reason, results cannot provide information on a causal relationship or a chronological order of the relationship between pain catastrophizing and the outcome variables.

Most current treatment modalities in PDN are one-dimensional; they solely focus on the disease and/or pain itself and rehabilitation interventions mainly improve physical fitness. This study shows that it is important not only to objectify the daily activity level of a patient with PDN, but also to focus on the perceived change in a patients' activity level. This knowledge can have great implications for the management of patients with PDN, as treatment modalities that focus on pain or physical activity alone most likely will not suffice.

In conclusion, neuropathic pain is a complex and multidimensional condition, which often has a major negative impact on daily life, both physically and mentally. The present study illustrates that patients with PDN who engage in catastrophic thinking experience a loss in physical activity, increased perceived disability, and lesser QOL. Based on our results, we stress the importance of integration of psychological aspects such as pain catastrophizing in the treatment of PDN.

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DISCLOSURE

The authors have nothing to disclose.

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