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Sensory Pain Qualities in Neuropathic Pain

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Abstract

The qualities of chronic neuropathic pain (NeP) may be informative about the different mechanisms of pain. We previously developed a 2-factor model of NeP that described an underlying structure among sensory descriptors on the Short-Form McGill Pain Questionnaire (SF-MPQ). The goal of this study was to confirm the correlated 2-factor model of NeP. Individual descriptive scores from the SF-MPQ were analyzed. Confirmatory factor analysis (CFA) was used to test a correlated 2-factor model. Factor 1 (stabbing pain) was characterized by high loadings on stabbing, sharp, and shooting sensory items; factor 2 (heavy pain) was characterized by high loadings on heavy, gnawing, and aching items. Results of the CFA strongly supported the correlated 2-factor model.

Keywords

Diabetic peripheral neuropathy; neuropathic pain; postherpetic neuralgia; confirmatory factor analysis; regularized regression; pain qualities

Introduction

While chronic neuropathic pain (NeP) is a multidimensional experience, the primary focus of most clinical therapeutic trials for NeP is pain intensity (magnitude or quantity). However, other dimensions of pain such as affect (or unpleasantness), location, timing, quality, and interference with activity may be as important as pain intensity in therapeutic trials and in the characterization of chronic pain states. These pain dimensions may directly inform researchers about pain mechanisms and treatment responsiveness to the active agent

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Disclosures

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or placebo. Unfortunately, these other dimensions of pain are rarely the focus of therapeutic trials for chronic NeP.

Pain qualities (eg, hot, stabbing, aching), in particular, have become the focus of recent research in chronic pain, as preliminary evidence indicates that different pain sensations may reflect different pain mechanisms.¹⁰ Improved understanding of the relationship between the sensations of qualities of pain and their underlying mechanisms would advance our knowledge of the causes of different chronic pain conditions. Furthermore, if certain pain qualities are preferentially affected by a particular therapy, these qualities may provide clinicians a basis for choosing between a multitude of available treatment options. These features of pain qualities have led investigators to call for more research into their characterization for specific pain treatments and perhaps for distinguishing pain mechanisms.¹⁸

We recently demonstrated that a correlated 2-factor model of NeP described an underlying structure among sensory descriptors on the Short-Form McGill Pain Questionnaire (SF-MPQ).⁹ The first factor, stabbing pain, was characterized by a high percentage of patients using the words stabbing, sharp, and shooting to describe their pain experiences. The second factor, heavy pain, was characterized by high use of the terms heavy, gnawing, and aching to describe pain. Specific and differential analgesic responses to lidocaine were identified from the pain factors. Compared with patients with low levels of heavy pain, patients with high levels of heavy pain factor had significantly greater reduction in pain intensity, as measured by a visual analog scale (VAS), in response to intravenous lidocaine but not in response to placebo.⁹ This study was limited by the small sample size ($n = 71$) and heterogeneity of the suspected NeP conditions. We sought to confirm this 2-factor model of NeP in this study of a large cohort of patients with 1 of 2 common NeP conditions, diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN), who were treated with pregabalin in randomized controlled clinical trials. NeP associated with DPN is present in approximately 11 to 26% of patients with diabetes.^{8,11,13,24} PHN occurs in 7 to 27% of patients who develop symptomatic reactivation of latent *Varicella zoster* virus, with the elderly at especially high risk. As many as 50% of patients aged 70 or older will have persistent pain 6 months after healing of the acute rash.^{16,22,27,35}

Methods

Patients and Treatment

Patient data from 6 DPN,^{1,21,25,28,29,32} 4 PHN,^{12,30,31,33} and 1 combined DPN/PHN¹⁴ randomized, placebo-controlled clinical trials were selected for this study. These data were limited to fixed doses of pregabalin 150, 300, or 600 mg/d or placebo (Table 1).

Assessments

The SF-MPQ was administered to patients at the baseline visit in each study. The questionnaire sections included in this analysis were: (a) the pain descriptors and (b) the VAS. To maintain consistency across the studies, SF-MPQ individual descriptor scores were analyzed for English-speaking patients only. For SF-MPQ pain descriptors, the patient rated the intensity of each type of pain that he/she had experienced over the past week on a 4-point intensity scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). The VAS provided a rating of overall pain during the past week; the patient placed a hash mark across a 100-mm line to indicate the intensity of the pain from left (0 mm = “no pain”) to right (100 mm = “worst possible pain”).

Statistical Methods

All randomized, intent-to-treat patients with nonmissing SF-MPQ scores at baseline were analyzed. SF-MPQ individual descriptor scores were summarized by disease and treatment groups.

Confirmatory Factor Analysis

Confirmatory factor analysis (CFA)¹⁹ was used to test the correlated 2-factor measurement structure of pain originally reported in the literature.⁹ Accordingly, the first factor, stabbing pain, was characterized by a set of three descriptors: stabbing, sharp, and shooting. The second factor, heavy pain, was characterized by a different set of three descriptors: heavy, gnawing, and aching. The covariance between the stabbing and heavy pain factors were also estimated. The diagonally weighted least squares estimator was used to take account of ordinal item distributions²³; missing-at-random was assumed. All available data were used to estimate the model.

Results

Patient Disposition and Pain Descriptors

The pooled population (N = 2,516) was modified owing to clarification of an SF-MPQ descriptor (at least one non-missing English-only SF-MPQ descriptor). In order to maintain consistency across the analysis, SF-MPQ individual descriptive scores are described and analyzed only for English-speaking patients. Thus, the final analyzed cohort (n = 2,267) included patients with DPN (n = 1,250) and PHN (n = 1,017, Table 2). Baseline demographics were comparable across the treatment groups in the pooled population. The baseline mean VAS scores were similar in the pregabalin (68.98) and placebo (70.00) groups.

The percentage of patients who completed the SF-MPQ and selected each of the pain descriptors at the time of randomization within the studies, separately for treatment group and disease group, is given in Figure 1. At least 50% of patients with either DPN or PHN chose most of the pain descriptors. The aching, hot-burning, sharp, throbbing, shooting, stabbing, and tiring-exhausting descriptors were chosen by at least 75% of all patients at randomization, which suggests that these pain descriptors are characteristic of painful peripheral neuropathy in general. Among the patients with PHN only, the tiring-exhausting, tender, aching, hot-burning, and sharp descriptors were chosen by at least 75% of patients in each treatment group (placebo and pregabalin) at randomization (Figure 1).

Confirmatory Factor Analysis

The correlated 2-factor model of pain was sufficient to explain the observed covariance structure among SF-MPQ sensory items.⁹ Factor 1, labeled as “stabbing pain quality,” was characterized by high factor loadings on stabbing, sharp, and shooting sensory descriptors. Factor 2, labeled as “heavy pain quality,” was characterized by high factor loadings on heavy, gnawing, and aching sensory descriptors. “Throbbing” and “splitting” qualities appeared to load equally on both factors; thus, these 2 items lacked the trait discriminant validity and were not used to measure the 2 factors.

A CFA on the DPN, PHN, and DPN/PHN pooled studies was performed separately to test and confirm the 2-factor structure (sharp pain, heavy pain, and the pain qualities that grouped with each) previously reported.⁹ As a competing model, a unidimensional pain factor model (1-factor model) was also tested. The CFA independently and strongly supported the correlated 2-factor structure in terms of absolute fit and relative fit. Absolute fit statistics were within the acceptable range (ie, root mean square error of approximation

≤ 0.07 , comparative fit index ≥ 0.99 , and Tucker-Lewis Index ≥ 0.99 ; Table 3).¹⁷ In latent variable modeling, it is customary to inspect multiple indices of fit because each index has its own strengths and limitations.⁴

The correlation between the heavy and stabbing factors was moderate (0.67/0.70/0.68 for the DPN/PHN/combined data). In terms of relative and absolute model fit, the correlated 2-factor model held in both samples (Table 4).

Discussion

Our results confirm that in a large cohort of patients with either DPN or PHN, factor analysis of the 11 baseline SF-MPQ sensory pain qualities reveals a 2-factor model of pain: (1) stabbing pain quality (utilizing stabbing, sharp, and shooting pain descriptors) and (2) heavy pain quality (utilizing heavy, gnawing, and aching pain descriptors). Interestingly, the quality of ‘throbbing’ did not discriminate between the 2 factors. As an independent and large sample, these results confirm our prior work that was performed in a much smaller and more heterogeneous group of patients with suspected NeP.⁹

Similar pain factors were described for patients with localized osteoarthritis (OA).³⁴ “Stabbing” was used as a descriptor of pain by 18% of patients with localized OA who completed the MPQ, as opposed to 4% of patients with generalized OA or rheumatoid arthritis (RA). While heavy pain was not explicitly measured in this study, terms such as “cramping” and “pressing” were used by patients with localized OA more frequently than by patients with RA or generalized OA. The authors suggested that specific pain descriptors may be sufficiently sensitive to discriminate between related painful conditions, but their sample size was too small to substantiate this claim.³⁴

The 2-factor pain quality structure is important because it may inform us about mechanisms of neuropathic pain in general. It is notable that the 2-factor structure coincides with distinctive pain sensations carried by A δ and C fibers. In particular, A δ fibers have been associated with the pain sensation described as acute or “first pain” akin to the stabbing pain factor in this study, whereas C fiber stimulation has been described as possessing pain qualities such as dull, slow, “second pain,”^{5,26} similar to the heavy pain factor described in this report. While we did not attempt to characterize the mechanisms associated with the stabbing and heavy factors in this study, and any association is admittedly speculative, future research should characterize the pain factor quality–mechanism relationships.

Limitations of our study are predominately due to the restricted number of pain qualities represented in the SF-MPQ. The SF-MPQ uses 11 words to characterize the sensory qualities of pain: throbbing, shooting, stabbing, sharp, cramping, gnawing, hot-burning, aching, heavy, tender, and splitting. Additionally, the SF-MPQ uses 4 affective qualities: tiring-exhausting, sickening, fearful, and punishing-cruel. We did not evaluate the affective qualities in this study. Several instruments have been developed to specifically characterize pain qualities in NeP including, but not limited to, the Neuropathic Pain Scale,¹⁵ Leeds Assessment of Neuropathic Symptoms and Signs,³ Neuropathic Pain Symptom Inventory,⁷ Neuropathic Pain Diagnostic Questionnaire,⁶ and Neuropathic Pain Questionnaire²⁰ (and its Short Form²). While useful, several of these instruments do not address the non-traditional pain qualities found in the heavy pain factor such as aching, dull, or gnawing. However, the additional pain descriptors in these instruments may enhance the content validity of pain scores estimated from our 2-factor model. Furthermore, the additional pain quality descriptors may allow for identification of distinctive factor structures for DPN and PHN. In this study, we did not find a different structure for the 2 NeP conditions—despite the clearly different initial conditions—that supported the generalizability of the proposed 2-

dimensional measure of pain in independent samples. Finally, we note that the population size of this study may be large with regards to the inherent variability of some descriptors, which could lead to overfitting of some factors in the analysis. However, the sample size for this study needed to be large enough to adequately power the CFA for interpretable results.

The specific qualities of pain may be indicative of pain mechanisms and may eventually guide physicians toward the most effective therapies for particular conditions. We previously described a 2-factor structure for the qualities of general neuropathic pain in a small study.⁹ In this report, a unidimensional conceptualization of pain (ranging from low to high levels) has been rejected. Instead, our results confirm the two related dimensions of pain (heavy and stabbing) in a large cohort of patients with two distinct painful neuropathies (DPN and PHN). In clinical settings, one patient may present a high level of heavy pain accompanied by a low level of stabbing pain whereas another patient may present high levels of both heavy and stabbing pain. Future studies should investigate whether this two dimensional representation of pain qualities is associated with distinctive pain mechanisms and treatment responsiveness to therapeutic agents, as well as the generalizability of two dimensional representation of pain in non-neuropathic populations.

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References

1. Arezzo JC, Rosenstock J, Lamoreaux L, Pauer L. Efficacy and safety of pregabalin 600 mg/d for treating painful diabetic peripheral neuropathy: a double-blind placebo-controlled trial. *BMC Neurol.* 2008; 8:33. [PubMed: 18796160]
2. Backonja MM, Krause SJ. Neuropathic pain questionnaire--short form. *The Clinical journal of pain.* 2003; 19:315–316. [PubMed: 12966257]
3. Bennett M. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs. *Pain.* 2001; 92:147–157. [PubMed: 11323136]
4. Bentler PM. Comparative fit indexes in structural models. *Psychological bulletin.* 1990; 107:238–246. [PubMed: 2320703]
5. Bishop, GH.; Landau, WM.; Jones, MH. *Science.* Vol. 128. New York, NY: 1958. Evidence for a double peripheral pathway for pain.; p. 712-714.
6. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, Cunin G, Fermanian J, Ginies P, Grun-Overdyking A, Jafari-Schluep H, Lanteri-Minet M, Laurent B, Mick G, Serrie A, Valade D, Vicaute E. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain.* 2005; 114:29–36. [PubMed: 15733628]
7. Bouhassira D, Attal N, Fermanian J, Alchaar H, Gautron M, Masquelier E, Rostaing S, Lanteri-Minet M, Collin E, Grisart J, Boureau F. Development and validation of the Neuropathic Pain Symptom Inventory. *Pain.* 2004; 108:248–257. [PubMed: 15030944]
8. Boulton AJ, Knight G, Drury J, Ward JD. The prevalence of symptomatic, diabetic neuropathy in an insulin-treated population. *Diabetes Care.* 1985; 8:125–128. [PubMed: 3996169]
9. Carroll IR, Younger JW, Mackey SC. Pain quality predicts lidocaine analgesia among patients with suspected neuropathic pain. *Pain Med.* 2010; 11:617–621. [PubMed: 20210867]
10. Chang PF, Arendt-Nielsen L, Graven-Nielsen T, Svensson P, Chen AC. Comparative EEG activation to skin pain and muscle pain induced by capsaicin injection. *Int J Psychophysiol.* 2004; 51:117–126. [PubMed: 14693361]

11. Davies M, Brophy S, Williams R, Taylor A. The prevalence, severity, and impact of painful diabetic peripheral neuropathy in type 2 diabetes. *Diabetes Care*. 2006; 29:1518–1522. [PubMed: 16801572]
12. Dworkin RH, Corbin AE, Young JP Jr, Sharma U, LaMoreaux L, Bockbrader H, Garofalo EA, Poole RM. Pregabalin for the treatment of postherpetic neuralgia: a randomized, placebo-controlled trial. *Neurology*. 2003; 60:1274–1283. [PubMed: 12707429]
13. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, Wilson DM, O'Brien PC, Melton LJ 3rd, Service FJ. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. *Neurology*. 1993; 43:817–824. [PubMed: 8469345]
14. Freynhagen R, Strojek K, Griesing T, Whalen E, Balkenohl M. Efficacy of pregabalin in neuropathic pain evaluated in a 12-week, randomised, double-blind, multicentre, placebo-controlled trial of flexible- and fixed-dose regimens. *Pain*. 2005; 115:254–263. [PubMed: 15911152]
15. Galer BS, Jensen MP. Development and preliminary validation of a pain measure specific to neuropathic pain: the Neuropathic Pain Scale. *Neurology*. 1997; 48:332–338. [PubMed: 9040716]
16. Gilden DH, Kleinschmidt-DeMasters BK, LaGuardia JJ, Mahalingam R, Cohrs RJ. Neurologic complications of the reactivation of varicella-zoster virus. *N Engl J Med*. 2000; 342:635–645. [PubMed: 10699164]
17. Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling*. 1999; 6:1–55.
18. Jensen MP. Using pain quality assessment measures for selecting analgesic agents. *The Clinical journal of pain*. 2006; 22:S9–13. [PubMed: 16344610]
19. Joreskog KG. A general approach to confirmatory maximum likelihood factor analysis. *Psychometrika*. 1969; 34:183–202.
20. Krause SJ, Backonja MM. Development of a neuropathic pain questionnaire. *The Clinical journal of pain*. 2003; 19:306–314. [PubMed: 12966256]
21. Lesser H, Sharma U, LaMoreaux L, Poole RM. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology*. 2004; 63:2104–2110. [PubMed: 15596757]
22. MacDonald BK, Cockerell OC, Sander JW, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. *Brain*. 2000; 123(Pt 4): 665–676. [PubMed: 10733998]
23. Muthen, LK.; Muthen, BO. *Mplus User's Guide* (1998-2010). Sixth Edition ed.. Muthen & Muthen; Los Angeles, CA: 2010.
24. Partanen J, Niskanen L, Lehtinen J, Mervaala E, Siitonen O, Uusitupa M. Natural history of peripheral neuropathy in patients with non-insulin-dependent diabetes mellitus. *N Engl J Med*. 1995; 333:89–94. [PubMed: 7777034]
25. [June 28] Pfizer: Protocol No. 1008-040: A placebo-controlled trial of pregabalin and amitriptyline for treatment of painful diabetic peripheral neuropathy. Available at: http://www.clinicalstudyresults.org/documents/company-study_1952_0.pdf
26. Ploner M, Gross J, Timmermann L, Schnitzler A. Cortical representation of first and second pain sensation in humans. *Proceedings of the National Academy of Sciences of the United States of America*. 2002; 99:12444–12448. [PubMed: 12209003]
27. Ragozzino MW, Melton LJ 3rd, Kurland LT, Chu CP, Perry HO. Population-based study of herpes zoster and its sequelae. *Medicine (Baltimore)*. 1982; 61:310–316. [PubMed: 6981045]
28. Richter RW, Portenoy R, Sharma U, Lamoreaux L, Bockbrader H, Knapp LE. Relief of painful diabetic peripheral neuropathy with pregabalin: a randomized, placebo-controlled trial. *J Pain*. 2005; 6:253–260. [PubMed: 15820913]
29. Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain*. 2004; 110:628–638. [PubMed: 15288403]
30. Sabatowski R, Galvez R, Cherry DA, Jacquot F, Vincent E, Maisonobe P, Versavel M. Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia:

- results of a randomised, placebo-controlled clinical trial. *Pain*. 2004; 109:26–35. [PubMed: 15082123]
31. Sharma U, Young JP Jr, LaMoreaux L, Emir B, Murphy TK, Siffert J. Efficacy, safety, and tolerability of pregabalin treatment for neuropathic pain: Findings from the analysis of 10 randomized clinical trials. *Eur J Neurology*. 2005; 12:196–197.
 32. Tolle T, Freynhagen R, Versavel M, Trostmann U, Young JP Jr. Pregabalin for relief of neuropathic pain associated with diabetic neuropathy: a randomized, double-blind study. *Eur J Pain*. 2008; 12:203–213. [PubMed: 17631400]
 33. van Seventer R, Feister HA, Young JP Jr, Stoker M, Versavel M, Rigaudy L. Efficacy and tolerability of twice-daily pregabalin for treating pain and related sleep interference in postherpetic neuralgia: a 13-week, randomized trial. *Curr Med Res Opin*. 2006; 22:375–384. [PubMed: 16466610]
 34. Wagstaff S, Smith OV, Wood PH. Verbal pain descriptors used by patients with arthritis. *Ann Rheum Dis*. 1985; 44:262–265. [PubMed: 3985692]
 35. Watson CP, Evans RJ, Watt VR, Birkett N. Post-herpetic neuralgia: 208 cases. *Pain*. 1988; 35:289–297. [PubMed: 2852344]

Perspective

This article validates a model that describes the qualities of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia. These data suggest that specific pain qualities may be associated with pain mechanisms or may be useful for predicting treatment response.

Figure 1.
Percent of patients in each disease group that chose specific pain descriptors on the Short-Form McGill Pain Questionnaire at baseline.

Table 1

Studies that have evaluated pregabalin in patients with painful DPN and PHN.

Study	Evaluate Treatment Arms	Endpoint Pain	Sensory	Affective	Total
DPN					
Richter et al ²⁸	Pregabalin 150 mg/d (n = 79) vs placebo (n = 82)	NS	NS	NS	NS
	Pregabalin 600 mg/d (n = 82) vs placebo (n = 82)	<0.001	<0.001	0.0014	<0.001
Lesser et al ²¹	Pregabalin 300 mg/d (n = 81) vs placebo (n = 97)	<0.001	<0.001	<0.001	<0.001
	Pregabalin 600 mg/d (n = 81) vs placebo (n = 97)	<0.001	<0.001	<0.001	<0.001
Pfizer Protocol No. 1008-040 ²⁵	Pregabalin 600 mg/d (n = 86, n = 25 SF-MPQ) vs placebo (n = 80, n = 24 SF-MPQ)	NS	NS	NS	NS
Rosenstock et al ²⁹	Pregabalin 300 mg/d (n = 75) vs placebo (n = 69)	<0.001	0.0060	0.0054	0.0033
Tölle et al ³²	Pregabalin 150 mg/d (n = 96) vs placebo (n = 93)	NS	NS	0.0430	NS
	Pregabalin 300 mg/d (n = 75) vs placebo (n = 93)				
	Pregabalin 600 mg/d (n = 75) vs placebo (n = 93)				
Arezzo et al ¹	Pregabalin 600 mg/d (n = 80) vs placebo (n = 83)	<0.001	NS	NS	NS
PHN					
Sharma et al ³¹	Pregabalin 150 mg/d (n = 82) vs placebo (n = 87)	NS	NS	NS	NS
Sabatowski et al ³⁰	Pregabalin 150 mg/d (n = 81, n = 39 SF-MPQ) vs placebo (n = 81, n = 38 SF-MPQ)	0.0002	NS	NS	NS
	Pregabalin 300 mg/d (n = 76, n = 31 SF-MPQ) vs placebo (n = 81, n = 38 SF-MPQ)	0.0001	NS	NS	NS
Dworkin et al ¹²	Pregabalin 300 mg/d (n = 76, n = 31 SF-MPQ) vs placebo (n = 81, n = 38 SF-MPQ)	0.0001			
	Pregabalin 600 mg/d (n = 76, n = 31 SF-MPQ) vs placebo (n = 81, n = 38 SF-MPQ)	0.0001			
van Seventer et al ³³	Pregabalin 150 mg/d (n = 74) vs placebo (n = 78)	0.0213	0.0069	0.0461	0.0077
	Pregabalin 300 mg/d (n = 76) vs placebo (n = 78)				
	Pregabalin 600 mg/d (n = 76) vs placebo (n = 78)				

Study	Evaluable Treatment Arms	Endpoint Pain	Sensory	Affective	Total
DPN/PHN Mixed					
Freynhagen et al ¹⁴	Fixed pregabalin 600 mg/d (n = 128) vs placebo (n = 62)	<0.001	NS	NS	NS
	Flexible pregabalin (n = 139) vs placebo (n = 62)	0.002	NS	NS	NS

Abbreviations: DPN, diabetic peripheral neuropathy; NS, not significant; PHN, postherpetic neuralgia; SF-MPQ, Short-Form McGill Pain Questionnaire.

Table 2

Baseline demographics of the pooled study population

	Pregabalin			Placebo		
	Male	Female	Total	Male	Female	Total
n	785	661	1446	433	388	821
Age						
Mean, (SD)	62.9 (11.5)	64.3 (12.7)	63.5 (12.1)	63.5 (11.9)	63.4 (13.1)	63.5 (12.5)
Range	21 – 90	18 – 100	18 – 100	27 – 90	26 – 89	26 – 90
Race, n (%)						
White	732 (93.2)	613 (92.7)	1345 (93.0)	400 (92.4)	350 (90.2)	750 (91.4)

Abbreviations: SD, standard deviation.

Table 3

Confirmatory Factor Analysis Results for DPN, PHN, and Combined Data

Population	Model	Chi-Square	p-Value	RMSEA	CFI	TLI
DPN	1-factor	424.76	<0.0001	0.22	0.87	0.85
	Correlated 2-factor	39.67	<0.0001	0.07	0.99	0.99
PHN	1-factor	230.37	<0.0001	0.17	0.87	0.85
	Correlated 2-factor	11.45	NS	0.03	1.00	1.00
Combined	1-factor	601.16	<0.0001	0.19	0.87	0.85
	Correlated 2-factor	44.82	<0.0001	0.05	0.99	0.99

Abbreviations: RMSEA, root mean square error of approximation; CFI, comparative fit index; TLI, Tucker-Lewis Index; DPN, diabetic peripheral neuropathy; PHN, postherpetic neuralgia; NS, not significant.

Table 4

Standardized Parameter Estimates For DPN, PHN, and Combined Data

Items	Factor 1 Stabbing Pain Quality	Factor 2 Heavy Pain Quality
Stabbing	0.81/0.73/0.77 [*]	0
Sharp	0.79/0.76/0.78 [*]	0
Shooting	0.80/0.76/0.78 [*]	0
Heavy	0	0.79/0.87/0.83 [*]
Gnawing	0	0.55/0.43/0.48 [*]
Aching	0	0.65/0.58/0.62 [*]

Abbreviations: DPN, diabetic peripheral neuropathy; PHN, postherpetic neuralgia.

^{*} DPN/PHN/Combined data.