ISSN: 2476-5279; International Journal of Musculoskeletal Pain Prevention. 2025;10(1): 1177-1186.

The Effectiveness of Cognitive-Behavioral Therapy on Recurrent Negative Thoughts, Anxiety Sensitivity, and Emotional Adjustment in Diabetic Neuropathy Pain

ARTICLEINFO

Article Type
Original Article

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How to cite this article

Madani F, Haghighat Bayan N, Mahmoudi M, Saeidi Moghadam F, Savabi Niri V . The Effectiveness of Cognitive-Behavioral Therapy on Recurrent Negative Thoughts, Anxiety Sensitivity, and Emotional Adjustment in Diabetic Neuropathy Pain. IJMPP. 2025; 10(1): 1177-1186.

ABSTRACT

Aims: Diabetic Neuropathy Pain (DNP) is a chronic condition that arises from nerve damage caused by prolonged hyperglycemia. It leads to burning, tingling, and sharp pain, primarily in the extremities. This study examines the effectiveness of Cognitive-Behavioral Therapy (CBT) in mitigating recurrent negative thoughts, reducing anxiety sensitivity, and enhancing emotional adjustment in individuals with DNP.

Method and Materials This study employed a quasi-experimental pre-test-post-test design with a control group, involving 36 patients with DNP from Ardabil clinics located in Ardabil, Iran in 2024. Patients were purposively sampled and randomly assigned to experimental (n = 18) and control (n = 18) groups. The experimental group underwent eight 90-minute CBT sessions, while the control group received no intervention. Data were gathered using the Repetitive Negative Thinking Questionnaire (RNTQ), Anxiety Sensitivity Index-3 (ASI-3), and Emotional Adjustment Measure (EAM), and analyzed via MANCOVA in SPSS-27.

Findings: The results demonstrated that CBT significantly improves emotional adjustment ($F = 49.46$) and reduces recurrent negative thoughts ($F = 45.41$), as well as physical ($F = 52.27$), cognitive ($F = 59.61$), and social dimensions of anxiety sensitivity ($F = 38.34$) in individuals with DNP ($P < 0.001$).

Conclusion: The findings highlight CBT's transformative impact on the psychological resilience of DNP patients, fostering adaptive emotional regulation and diminishing maladaptive thought patterns. By addressing the interconnected dimensions of anxiety sensitivity and emotional adjustment, CBT offers a pathway to holistic pain management, emphasizing its potential as a cornerstone in the psychological care of chronic pain conditions.

Keywords: Diabetic Neuropathy Pain, Cognitive-Behavioral Therapy, Recurrent Negative Thoughts, Anxiety Sensitivity, Emotional Adjustment

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Article History
Received: Dec 20, 2024
Accepted: Feb 02, 2025
ePublished: Mar 20, 2025

Introduction

Diabetic Neuropathy Pain (DNP) is a debilitating complication of diabetes that arises from nerve damage caused by prolonged hyperglycemia [1]. It is characterized by persistent and severe pain, often described as burning, stabbing, or tingling, that significantly impacts patients' physical and psychological well-being [2]. Affecting up to 50% of individuals with diabetes, DNP represents a critical challenge in diabetes management due to its chronic nature and resistance to conventional pain treatments [3]. The pathophysiology of DNP involves complex mechanisms, including metabolic dysregulation, oxidative stress, and inflammatory processes, which lead to peripheral nerve dysfunction [4]. While these biological factors are central to the onset of pain, the experience of DNP is profoundly influenced by psychological and emotional aspects [5]. Individuals with DNP often experience comorbid conditions such as depression, anxiety, and stress, which exacerbate the perception of pain and hinder effective management [6]. This interplay between physical and psychological symptoms highlights the need for holistic approaches to treatment [7].

Characterized by persistent, severe pain, and psychological challenges, including depression, anxiety, and stress often accompany it [8]. Among these psychological factors, Recurrent Negative Thoughts (RNT)—defined as repetitive, intrusive,

and uncontrollable patterns of negative thinking—play a pivotal role in exacerbating the experience of pain and contributing to emotional distress [9]. These thoughts often revolve around themes of hopelessness, self-doubt, and fear, creating a vicious cycle that intensifies both physical and psychological suffering [10]. Recurrent Negative Thoughts are a common cognitive phenomenon in chronic pain conditions, including DNP [11]. It encompasses processes like rumination, worry, and catastrophizing, which have been shown to heighten pain perception and hinder effective coping strategies [12]. For individuals with DNP, RNT can amplify their pain sensitivity, reduce their ability to manage symptoms, and interfere with adherence to treatment regimens [13]. Furthermore, these negative cognitive patterns are closely linked to increased emotional dysregulation, further complicating the management of chronic pain [14]. Anxiety Sensitivity (AS), defined as the fear of anxiety-related sensations stemming from the belief that they signify harm or danger, has been identified as a crucial factor influencing the experience of chronic pain [15]. AS heightens emotional and physiological responses to pain, intensifying its perception and broadening its impact on daily life. This heightened sensitivity is particularly significant in chronic pain conditions such as DNP [16]. For individuals with elevated AS, normal pain sensations may be misinterpreted as indicators of serious or worsening health issues, triggering a cycle of fear and avoidance [17]. This cycle exacerbates psychological distress, promotes hypervigilance, and fosters maladaptive behaviors, all of which amplify the subjective experience of pain [18]. Over time, these effects contribute to poor emotional adjustment, reduced physical activity, and a diminished quality of life [19]. While the relationship between AS and chronic pain is well-documented in other conditions, its specific role in DNP has not been thoroughly explored [20]. Evidence suggests that AS may worsen the psychological burden of DNP by increasing tendencies toward worry, catastrophizing, and other maladaptive cognitive responses to pain [21]. Consequently, targeting AS in individuals with DNP offers a promising opportunity to improve both psychological and physical outcomes [22].

Emotional adjustment, defined as the ability to regulate emotional responses and sustain psychological balance in challenging situations, plays a pivotal role in determining how individuals navigate the difficulties of chronic pain [23]. Inadequate emotional adjustment can intensify the perception of pain, weaken coping mechanisms, and compromise adherence to treatment plans [24]. For individuals with DNP, emotional adjustment is frequently disrupted by the dual burden of managing a chronic illness and enduring the constant discomfort of neuropathic pain [25]. Difficulty in emotional regulation can lead to heightened feelings of hopelessness, frustration, and fear, creating a negative cycle that exacerbates both psychological distress and the experience of pain [26]. On the other hand, those who develop effective emotional adjustment strategies are better equipped to manage their pain, preserve functional abilities, and enhance their overall quality of life [23]. Although the importance of emotional adjustment in chronic pain management is increasingly recognized, its specific influence on DNP remains underexplored [27]. Emotional adjustment is shaped by personal factors, such as resilience and coping skills, and external factors, including social support and access to appropriate care [28]. Focusing on emotional adjustment in individuals with DNP offers a promising avenue for improving psychological health and alleviating the broader impact of this condition [25].

Traditional pharmacological treatments for DNP, such as analgesics and anticonvulsants, often provide limited relief and are associated with adverse side effects, leaving many patients in search of alternative approaches [29]. This has led to growing interest in non-pharmacological interventions that address both the physical and psychological dimensions of DNP [30]. Cognitive-Behavioral Therapy (CBT) is an evidence-based psychological intervention that identifies and alters maladaptive thought patterns and behaviors [31]. By addressing cognitive

distortions and promoting healthier coping mechanisms, CBT offers a comprehensive framework for managing chronic pain conditions, including DNP [32]. Chronic pain is not merely a physical experience; it is deeply intertwined with cognitive and emotional processes [33-34]. Negative thought patterns, such as catastrophizing and worry, as well as poor emotional adjustment, can intensify the perception of pain and reduce the effectiveness of pain management strategies [35]. Cognitive-Behavioral Therapy aims to break these cycles by equipping individuals with tools to challenge unhelpful thoughts, regulate emotions, and adopt adaptive behaviors [36-37].

The application of CBT in chronic pain management has been well-documented, with numerous studies demonstrating its effectiveness in reducing pain intensity, improving emotional well-being, and enhancing overall functioning. However, its specific application to DNP remains underexplored. Given DNP's unique interplay between physical and psychological factors, CBT holds significant promise as a holistic intervention. By addressing not only the sensory aspects of pain but also the cognitive-emotional factors that perpetuate it, CBT may offer a pathway to improved outcomes for individuals suffering from this condition. This study aims to explore the role of CBT in managing DNP, focusing on its potential to alleviate RNT, reduce anxiety sensitivity, and enhance emotional adjustment. By addressing these interconnected factors, CBT could emerge as a transformative tool in the holistic treatment of DNP, improving both psychological and physical well-being.

Method and Materials

The study is a randomized controlled clinical trial design with a pre-test-post-test framework and a control group. The statistical population included patients who suffered from DNP and were referred to pain and diabetes clinics in the Ardabil Province of Iran during November and December 2024. In this study, 36 patients with DNP were randomly allocated to the experimental and control groups (each group consisted of 18 patients). The sample size was calculated based on previous studies and by using G*Power software, adhering to the following parameters: effect size = 1.53, $\beta = 0.97$, and $\alpha = 0.05$. Inclusion criteria were consent to participate, having an age range of 18 to 50 years, no use of psychiatric medications, and no history of psychological interventions. Exclusion criteria were failure to complete questionnaire items, missing more than two therapy sessions, and exacerbation of pain during the intervention.

All ethical considerations as signing informed consent form, maintaining the confidentiality of their personal information, and adhering to ethical principles in human research were fully observed. All collected data were entered into SPSS software version 27. Multivariate covariance analysis was used to analyze the obtained scores. The significance of the assumptions was considered at the level of 0.05.

In this study, the following instruments were used. The Repetitive Negative Thinking Questionnaire (RNTQ) was developed by McEvoy, Mahoney, and Moulds in 2010 and consists of 31 items to assess the frequency and intensity of repetitive negative thoughts [38]. Responses are scored on a 5-point Likert scale, ranging from 1 (Never) to 5 (Always), with higher scores indicating greater levels of repetitive negative thinking. The total score is calculated by summing responses across all items. The questionnaire has high reliability, with Cronbach's alpha coefficients ranging from 0.72 to 0.93 in the original study. For predictive validity, the RNTQ was correlated with the Beck Depression Inventory and Beck Anxiety Inventory, yielding correlation coefficients of 0.42 and 0.38, respectively, indicating significant associations with depression and anxiety [38]. In the current study, Cronbach's alpha coefficient for the RNTQ was calculated as 0.84, indicating good internal consistency and reliability in measuring repetitive negative thinking within the target population.

The Anxiety Sensitivity Index-3 (ASI-3) measures the level of worry related to various symptoms of anxiety [39]. This scale is deprived of the revised Anxiety Sensitivity

Index which comprises 18 items and evaluates anxiety sensitivity across three dimensions: physical concerns (6 items), cognitive concerns (6 items), and social concerns (6 items). Participants respond on a five-point Likert scale ranging from 0 (very little agree) to 4 (completely agree), with total scores ranging from 0 to 72. The ASI-3 demonstrates strong psychometric properties, with internal consistency coefficients ranging between 0.76 and 0.86 for physical concerns, 0.79 and 0.91 for cognitive concerns, and 0.73 and 0.86 for social concerns. Additionally, the scale has shown good convergent and divergent validity (39). In the present study, the internal consistency for the subscales was also confirmed, with Cronbach's alpha coefficients ranging from 0.84 to 0.90.

The Emotional Adjustment Measure (EAM) which developed by Rubio, Aguado, Hontangas, and Hernández [40] and used in this study to assess emotional adjustment. This questionnaire comprises 28 items scored on a 6-point Likert scale (ranging from "strongly agree = 1" to "strongly disagree = 6"). It measures individuals' tendencies to achieve balance, regulation, and emotional stability when faced with emotional and affective instability. Rubio et al. [40] reported correlations of this scale with the Eysenck Personality Inventory and the emotional adjustment subscale of the Big Five Personality Questionnaire as r = 0.86 and r = 0.77, respectively. They also reported a Cronbach's alpha reliability coefficient of 0.87. In the current study, the reliability coefficient for the EAM was found as 0.84, indicating satisfactory reliability for this questionnaire.

Before the treatment sessions, research questionnaires were distributed among the participants during the pre-test phase. Following the completion of the pre-test, the intervention group received CBT administered by the therapist over 8 sessions spanning two months, and each session lasted 90 minutes [41]. To address ethical considerations, the control group was informed that they would receive the desired treatment after one month and were advised to continue their standard medical care in the meantime. Once the treatment sessions for the intervention group were completed all participants took part in the post-test phase and completed the research questionnaires. To minimize dropout rates, all participants were asked during the initial interview to commit to attending all sessions throughout the program. This commitment was reinforced during the sessions, and the sense of solidarity developed among group members further contributed to maintaining group cohesion and preventing attrition. A summary of the CBT group sessions designed for patients with DNP is presented in Table 1.

Table 1) Characteristics of CBT Training Sessions (41)

Session	Target
1	Introducing and explaining the basic principles of CBT, introducing the fundamental concepts of therapy, setting the schedule of sessions, discussing the rules of sessions
2	Determining the agenda of the meeting, evaluating, formulating, conceptualizing the subjects' problems, and filling the formulation worksheet.
3	Determining the agenda of the meeting, selecting goals and determining treatment goals with the help of members, preparing notebooks for treatment and activity planning
4	Determining the agenda of the meeting, identifying and recognizing their thoughts, practicing recording thoughts, and assigning them to the patient as homework.
5	Changing and correcting one's thoughts, teaching the technique of creating a logical alternative, introducing the weekly activity registration form as homework
6	Diagnosing cognitive errors, examining evidence, and preparing confrontation cards
7	Graded task design, use of visual confrontation technique
8	Review of uncompleted activities, homework, and therapy notebooks, answers to members' questions, and summaries

Findings

The mean and standard deviation of the age of the intervention and control groups were 42.87±5.32 and 43.12±5.84, respectively. Table 2 presents the mean and standard deviation of pre-test and post-test scores for RNT, anxiety sensitivity, and emotional adjustment in DNP in both intervention and control groups. This table also includes the results of the Shapiro-Wilk test (S-W), which assessed the normality of the variable distributions in the two groups. The Shapiro-Wilk statistics are not significant for any of the variables, indicating that the distributions are normal (see Table 2).

Multivariate analysis of covariance was used to evaluate the efficacy of ACT on RNT, anxiety sensitivity, and emotional adjustment in DNP. The results of the Levin test to examine the homogeneity of variance of dependent variables in groups showed that the variance of RNT (F=1.59, P=0.195), anxiety sensitivity (F=1.95, P=0.214), and emotional adjustment (F=1.41, P=0.108) was equal in the groups. The results of the box test to evaluate the equality of the covariance matrix of dependent variables between the intervention and control groups also showed that the covariance matrix of the dependent variables is equal (Box M= 29.947, F=1.677, P=0.058). The significance of the box test is greater than 0.05, so this assumption is valid. Also, the results of the Chi-square-Bartlett test to examine the sphericity or significance of the relationship between RNT, anxiety sensitivity, and emotional adjustment showed that the relationship between them is significant (χ^2=119.04, df=14, P<0.01).

Another important assumption of multivariate analysis of covariance is the homogeneity of regression coefficients. It should be noted that the homogeneity test of regression coefficients was examined through the interaction of dependent variables and independent variables (intervention method) in the pre-test and post-test. The interaction of these pre-tests and post-tests with the independent variable was not significant and indicated the homogeneity of the regression slope. Therefore, this assumption also holds. Due to the establishment of multivariate analysis of covariance, the use of this test will be allowed. Then, to find out the differences between the groups, a multivariate analysis of covariance was performed (Table 3).

Table 2) Descriptive Indices of Study's Variables in Control and Experimental Groups

Variables		Groups	Mean	SD	S-W	P
Recurrent Negative Thoughts	Pre-test	Experimental	92.55	2.01	0.126	0.075
		Control	92.44	2.03	0.106	0.069
	Post-test	Experimental	87.89	3.34	0.098	0.051
		Control	92.66	1.97	0.205	0.071
Physical	Pre-test	Experimental	17.45	1.41	0.087	0.063
		Control	17.38	1.68	0.114	0.087
	Post-test	Experimental	14.43	1.84	0.138	0.059
		Control	17.50	1.54	0.096	0.084
Cognitive	Pre-test	Experimental	19.33	1.39	0.087	0.071
		Control	19.27	1.52	0.128	0.066
	Post-test	Experimental	15.94	1.91	0.119	0.052
		Control	19.38	1.84	0.088	0.091
Social	Pre-test	Experimental	15.27	1.63	0.110	0.060
		Control	15.33	1.53	0.094	0.055
	Post-test	Experimental	12.54	1.74	0.122	0.079
		Control	15.27	1.93	0.142	0.082
Emotional Adjustment	Pre-test	Experimental	84.66	3.21	0.095	0.052
		Control	84.78	3.04	0.093	0.061
	Post-test	Experimental	88.67	3.85	0.131	0.089
		Control	84.56	3.10	0.105	0.063

S-W: Shapiro-Wilk test; SD: Standard Deviation; P: P value

Table 3) The Results of Multivariate Analysis of Covariance on Mean Post-Test Scores

Test	Value	F	df	Error df	P	Effect Value
Pillai's Trace	0.697	11.480	5	25	<0.001	0.69
Wilks Lambda	0.303	11.480	5	25	<0.001	0.69
Hoteling Trace	2.296	11.480	5	25	<0.001	0.69
Roy's Largest Root	2.296	11.480	5	25	<0.001	0.69

According to Table 4, the results showed the effect of the independent variable on the dependent variables; In other words, intervention and control groups have a significant difference in at least one of the variables of RNT, anxiety sensitivity, and emotional adjustment, which according to the calculated effect size, 69% of the total variance of intervention and control "groups is due to the effect of the independent variable. Also, the test's statistical power is equal to 1, which indicates the adequacy of the sample size. However, to determine in which areas the difference is significant, a univariate analysis of the covariance test was used in the MANCOVA, the results of which are reported in Table 4.

Table 4) Results of Univariate Analysis of Covariance on the Mean of Post-Test Scores of Dependent Variables in Two Experimental and Control Groups

Variables	SS	SS Error	DF	MS	MS Error	F	P	Effect Value
Recurrent Negative Thoughts	2313.511	136.35	1	2313.511	4.70	45.41	<0.001	0.61
Physical	86.071	47.76	1	86.071	1.64	52.27	<0.001	0.64
Cognitive	108.521	52.79	1	108.521	1.82	59.61	<0.001	0.67
Social	62.681	47.41	1	62.681	1.63	38.34	<0.001	0.57
Emotional Adjustment	157.538	92.36	1	157.538	3.18	49.46	<0.001	0.63

According to the data presented in Table 4, the F-statistic is significant for recurrent negative thoughts (F = 45.41), physical (F = 52.27), cognitive (F = 59.61), social (F = 38.34), and emotional adjustment (F = 49.46) at the 0.001 significance level. These results demonstrate a significant difference between the groups in these variables. Additionally, based on the calculated effect size, 61% of the variance in RNT, 64% in physical adjustment, 67% in cognitive adjustment, 57% in social adjustment, and 63% in emotional adjustment can be attributed to the effects of the intervention. Consequently, it can be concluded that CBT significantly enhances emotional adjustment while reducing RNT and anxiety sensitivity across physical, cognitive, and social dimensions in individuals with DNP.

Discussion

This study examines the effectiveness of CBT in patients with DNP, focusing on reducing RNT, alleviating anxiety sensitivity, and improving emotional adjustment. Among these patients, the intervention significantly decreased the frequency and intensity of maladaptive thought patterns, helping them transition from ruminative and self-defeating tendencies to more adaptive and constructive cognitive frameworks. Recurrent negative thinking, often characterized by rumination and catastrophizing, is a common psychological response to chronic pain, exacerbating emotional distress and amplifying the pain experience [11]. CBT employs cognitive restructuring techniques that help patients identify and challenge maladaptive thoughts, replacing them with more balanced and constructive perspectives. This process not only diminishes the frequency of these negative thoughts but also weakens their emotional intensity, reducing their impact on the patient's mental state [35].

The reduction in RNT can also be attributed to CBT's focus on enhancing patients' metacognitive awareness and self-regulation skills [29]. Through strategies such as mindfulness training, patients learn to observe their thoughts without judgment, breaking the cycle of repetitive and self-defeating cognitive patterns [14]. This shift

fosters a sense of control over their mental processes, enabling them to reframe their responses to pain and stress more adaptively [33]. As a result, patients experience a decrease in the automaticity of negative thinking, allowing for a more constructive approach to managing their condition [30]. Additionally, CBT's structured and goal-oriented approach encourages patients to engage in behaviors that contradict negative thought patterns, such as problem-solving and positive self-affirmation [32]. These behavioral strategies reinforce cognitive changes by providing experiential evidence of their effectiveness, further reducing the tendency to engage in recurrent negative thinking. This combination of cognitive and behavioral interventions creates a comprehensive framework that addresses the root causes of negative thoughts, making CBT an effective tool for improving the psychological well-being of patients with DNP [31].

Furthermore, CBT demonstrated significant efficacy in reducing anxiety sensitivity across physical, cognitive, and social domains in patients with DNP. This reduction alleviated hypersensitivity to stressors and enhanced patients' adaptive capacity to manage pain-related anxieties more effectively. Anxiety sensitivity, often exacerbated by chronic pain, involves heightened awareness and fear of bodily sensations, cognitive distress, and social discomfort [16]. Cognitive Behavioral Therapy targets these fears through psychoeducation, helping patients understand the connection between their thoughts, emotions, and physiological responses [32]. This understanding diminishes the perceived threat of pain-related sensations; reducing physical anxiety sensitivity and helping patients reinterpret bodily signals more adaptively [41].

In the cognitive domain, CBT's emphasis on identifying and restructuring distorted thought patterns played a central role in reducing anxiety sensitivity. Patients with DNP often experience catastrophic thinking about their pain and its implications, which intensifies cognitive distress [29]. Cognitive Behavioral Therapy helps patients recognize these thought distortions and replace them with balanced, evidence-based perspectives. By diminishing catastrophic thinking, patients experience reduced cognitive anxiety sensitivity, enabling them to approach challenges with a calmer and more constructive mindset [36]. Finally, in the social domain, CBT reduces anxiety sensitivity by addressing fears related to judgment, social isolation, and perceived stigma associated with their condition [37]. Through role-playing, exposure techniques, and communication skills training, patients develop greater confidence in navigating social interactions [34]. This reduces their sensitivity to social stressors, fostering a sense of empowerment and reducing avoidance behaviors. Collectively, these cognitive, emotional, and behavioral changes highlight CBT's effectiveness in alleviating anxiety sensitivity and improving the overall psychological resilience of patients with DNP [30].

Additionally, CBT significantly improved emotional adjustment in patients with DNP, equipping them with the skills to effectively manage emotional responses and maintain psychological resilience in the face of chronic pain challenges. DNP often triggers heightened emotional responses, including frustration, sadness, and anxiety, which can amplify pain and hinder coping abilities. CBT provided patients with practical tools to identify and challenge maladaptive emotional responses, replacing them with healthier and more adaptive strategies [25]. By encouraging the recognition of unhelpful emotional triggers and reframing their interpretation, CBT facilitated better control over emotional reactions [37].

A critical mechanism through which CBT improved emotional adjustment was its emphasis on developing mindfulness and relaxation techniques [41]. These practices allowed patients to regulate their autonomic responses to pain-related stress, such as reducing hyperarousal and improving tolerance for discomfort [35]. As a result, patients experienced less emotional reactivity and greater psychological stability in the face of persistent pain. This enhanced ability to manage stress and maintain emotional equilibrium directly contributed to improved

emotional adjustment [32]. Additionally, CBT emphasized goal setting, positive reinforcement, and problem-solving, which helped patients regain a sense of agency and self-efficacy [36]. This empowerment enabled patients to engage actively in their pain management and adopt a proactive attitude toward their well-being [33]. By focusing on solutions rather than dwelling on pain, patients developed a more constructive outlook, fostering resilience and improving emotional adjustment. These comprehensive cognitive, emotional, and behavioral interventions make CBT a powerful tool for enhancing emotional well-being in individuals with DNP [29].

This study faced several limitations, including a small sample size, the absence of long-term follow-up to assess the sustainability of outcomes, and the use of a single geographic location, which may limit generalizability. Additionally, the lack of an active intervention for the control group and the absence of blinding could have introduced bias. To address these limitations, future research should focus on larger, more diverse populations with extended follow-up periods to evaluate the long-term efficacy of CBT. Practical applications include integrating CBT into standard DNP management protocols, providing specialized training for healthcare professionals, and exploring group therapy options to enhance cost-effectiveness and peer support. Combining CBT with other multidisciplinary approaches, such as pharmacological treatments and physiotherapy, can further enhance its impact, offering a holistic care model for DNP patients.

Conclusion

The results of this study underscore the profound benefits of CBT in addressing the psychological challenges associated with DNP. Cognitive Behavioral Therapy not only reduced RNT but also alleviated anxiety sensitivity across physical, cognitive, and social domains, fostering a significant improvement in emotional adjustment. These outcomes suggest that CBT equips patients with effective coping mechanisms to manage the multifaceted stressors of chronic pain, enhancing their overall psychological resilience and quality of life. Given its demonstrated effectiveness, integrating CBT into the standard treatment protocols for DNP patients could bridge the gap between physical and psychological care. This integration has the potential to holistically address the complex interplay of pain and psychological distress, offering patients a comprehensive approach to pain management. Future research should focus on long-term evaluations of CBT outcomes and explore its synergistic effects when combined with other therapeutic modalities.

Acknowledgment: The authors would like to thank all the patients who participated in this study.

Authors' Contribution: FM and NHB: Conceptualization and Supervision, MM and FSM; Methodology, VSN and FM; Investigation. All authors helped in writing, reviewing, and editing the original draft.

Conflict of Interest: There were no conflicts of interest among the authors.

Ethical Approval: Ethical principles in manuscript writing have been adhered to by the guidelines of the National Ethics Committee and the COPE regulations.

Funding: No funding.

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