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The Impact of Neuropathic Pain on Depression-A Systematic Review

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Abstract

Background

Neuropathic pain, affecting 3-17% of the general population, is associated with significant mental health implications, particularly depression and anxiety. This pain, stemming from nervous system damage, often leads to depressive symptoms due to its persistence and challenges in traditional treatment methods. Understanding this connection between neuropathic pain and depression is of utmost importance as one may lead to another and vice versa and is crucial for comprehensive pain management and mental health support.

Methodology

Two independent researchers with the keywords performed a comprehensive review search; 'neuropathic', 'neurological', 'depression' and 'mental health' on Scopus, CINAHL, Google Scholar, and PubMed. All studies that assessed neuropathic pain were included in this review. The outcome measure was depression measured using a Physical health questionnaire (PHQ-9).

Results

Seven eligible studies conducted from 2020 to 2024 were included in this review. The findings reported a strong association of neuropathic pain with depression-associated symptoms ($p<0.05$).

Conclusion

The synthesis of findings from diverse studies underscores the bi-directional relationship between neuropathic pain and depression, emphasizing the need for integrated approaches to pain management and mental health care.

Keywords

Anxiety, Depression, Mental Health, Pain.

Introduction

Neurological pain ranks as the 4th most painful pain, with approximately 9.8% prevalence of neuropathic pain from clinical examination[1]. Neuropathic pain affects about 3-17% of the general population[2]. It is defined as a complex and often devastating problem that arises due to injury or failure of the nervous system, causing chronic pain[3]. Various factors, including dementia, diabetes, infection or autoimmune disease, can cause this type of pain. Neuropathic pain differs from nociceptive pain caused by tissue damage or swelling and presents unique challenges due to its nature and resistance to traditional analgesic medications[4]. In recent years, researchers have become increasingly aware of the significant impact that neuropathic pain, particularly depression and anxiety symptoms, can have on mental health[5].

Depression is a mental illness that affects approximately 280 million people worldwide[6]. It is characterized by persistent low energy and a lack of interest in daily activities. Depression negatively impacts women and is associated with an increased risk of suicide, a significant public health problem[7]. In 2019, it ranked as the most important contributor to mental health-related disability. The effects of neuropathic pain extend beyond physical symptoms and often cause serious mental illness. People with neuropathic pain frequently report symptoms of depression, anxiety, and social isolation; this can exacerbate their pain and continue the cycle of dysfunction and disability[8]. Many valid tools assess the severity of depression; one of them is "The Patient Health Questionnaire-9 (PHQ-9)", which is a widely used self-report instrument designed to measure the severity of depression. By exploring the relationship between neuropathic pain and PHQ-9 scores, we can better understand the connection between body and mind[9]. The relationship between neuropathic pain and PHQ-9 scores is complex and bi-directional. Individuals with neuropathic pain are more likely to have depressive symptoms due to persistent pain, limitations in daily activities, and problems with pain management[10]. Suffering from persistent neuropathic pain can negatively impact a person's well-being and lead to feelings of hopelessness and helplessness that are hallmarks of depression. The interplay between physical and emotional states highlights the importance of a positive approach to pain management that addresses the emotional and psychological aspects of neuropathic pain. Given the high prevalence of neuropathic pain and its profound impact on mental health, there is a growing need to examine the relationship between neuropathic pain and PHQ-9 scores systematically. A systematic review offers a rigorous and

comprehensive approach to synthesizing existing evidence from observational studies, clinical trials, and cross-sectional investigations.

Methodology

In this review, we conducted a comprehensive search between 2020 and 2024 and included all the studies that assessed the relationship between "neuropathic pain" and "depression". Details of these research strategies are described below.

Search Strategy

The research proposal was reviewed and accepted by X Research Institute. We searched the English literature Scopus, CINAHL, Google Scholar, and PubMed to retrieve all relevant studies between 2020 and 2024. The keywords searched included the following terms: ***'neuropathic'***, ***'neurological'***, ***'depression'***, and ***'mental health'***, which are used to search English literature. A manual search was also conducted to identify items not found in the electronic search.

Selection of Studies

The inclusion criteria for studies were those conducted between 2020 and 2024 in patients with neuropathic disorders and depression; studies with PHQ- as an outcome measure were included in this review. All studies published in languages other than English and with different outcomes, full articles not available, were excluded from the review.

Data Extraction

Data extraction for this systematic review involved a qualitatively collecting relevant data from selected studies. Key details captured included the first author's name, year of publication, study design, sample size and characteristics, procedure, outcomes, and findings. The data extraction was performed by two independent researchers who rigorously reviewed the selected articles for data extraction (Table-1). (PRISMA) guidelines for Systematic Reviews and Meta-Analysis were followed in this study[11].

Results

In primary search, we found 2078 articles based on keywords related to our topic. Of those, 1148 were obtained after excluding the duplicate studies. Again, 407 articles were excluded based on study design and language, yielding 741. The independent researcher performed a rigorous evaluation of the articles, which excluded 718 articles due to differences in the target population and outcomes. The 23 retrieved articles were critically appraised, and 7 were included in this review. The number of initial studies and the detailed process for selecting appropriate studies are shown in Figure-1.

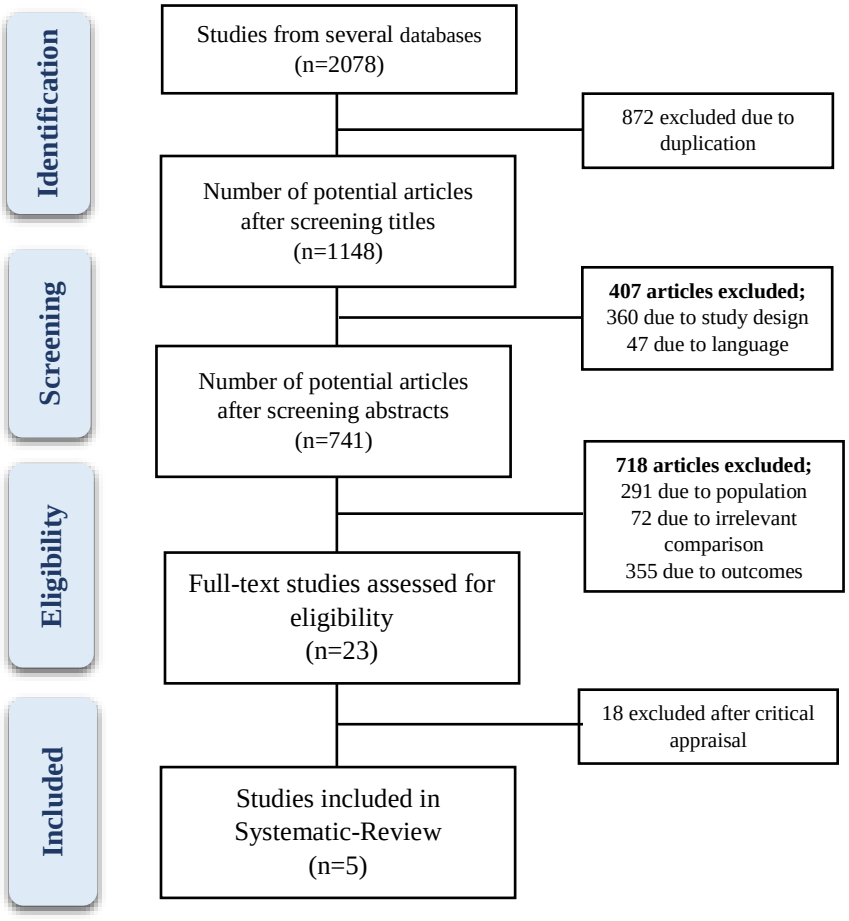

Figure-1 showing PRISMA Flow of Studies

The characteristics of participants across multiple studies investigating the relationship between depression and neurological disorders are summarized in Table-1. Each study employed a cross-

sectional or longitudinal design with varying age ranges and sample sizes, focusing on patients diagnosed with neuropathic pain, neurological disorders, or traumatic brain injury. Data collection procedures ranged from questionnaire assessments like the PHQ-9 to comprehensive evaluations of pain severity and psychiatric symptoms. Key findings highlighted significant associations between depression and neurological pain syndromes, with implications for screening tools like the PHQ-9 in identifying depressive symptoms within these patient populations. The diversity in study designs and outcome measures underscores this relationship's complexity and the need for a comprehensive review to synthesize these findings effectively.

Table-1 Characteristics of Participants

Authors, Year	Study Design	Sample size	Data Collection Procedure	Outcome	Findings
Sachau et al., 2023[12]	Cross-sectional study	n=3339 Participants aged 18-90 years with chronic neuropathic pain or complex regional pain syndrome	Data was collected from 2006-13 using a painDETECT software, which allowed patients to complete electronic questionnaires on their outpatient visits in primary care center	Patient Health Questionnaire-9	The findings showed that depression was strongly correlated with the type of neurological pain ($p<0.05$)
Sun et al., 2022[13]	Cross-sectional Study	n=277 Patients aged ≥18 years with neurological disorders	Out of 300, 290 questionnaires were returned, of which 277 patients complete further questionnaires for depression and neuropathic pain	Patient Health Questionnaire-9	The PHQ-9 has been shown to have good reliability and validity when screening for depression in patients with neurological diseases (0.839, $p<0.01$)
Suzuki et al., 2021[14]	Cross-sectional Study	n=551 Patients with neurological disorder with mean age 57.1±18.0 years	Data was collected from 2018-19 from 551individuals from outpatient clinics	Patient Health Questionnaire-9	Findings showed that central sensitization syndrome related symptoms were linked with pain severity and depressive symptoms ($p<0.001$)

Smith et al., 2020[15]	Cross-sectional Study	n=350 Patients aged ≥ 18 years with neurological pain (neuropathic, musculoskeletal, and orofacial) were assessed	Data was collected from 2016-17 from patients attending OFP clinic	Patient Health Questionnaire-9	Depression was associated with the neurological pain ($p<0.05$)
Teymoori et al., 2020[16]	Longitudinal Study	n=2137 Traumatic Brain Injury patients	Data was collected from the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI), of which 2137 patients completed the psychological outcome	Patient Health Questionnaire-9	49-67% of post-TBI, patients reported with depression and anxiety symptoms persisted over time

Risk of Bias in Studies

A low risk of bias was reported in funding and conflict of interest among four studies[12,13,15,16], except for one study[14], which showed a high risk of bias. For outcome assessment, all studies[12-16] showed a low risk of bias. In the domain of exposure assessment, two studies showed [14,15] low risks of bias, two studies[12,13] showed the unknown risk of bias, and one study[16] showed a high risk of bias. The details are mentioned in Table 2.

Table-2 Assessing Risk of Bias of Included Studies						
Author' Year	**Funding and Conflict of Interest**	**Outcome Assessment**	**Exposure Assessment**	**Confounding Factors**	**Attrition Bias**	**Analysis**
Sachau et al., 2023[12]	+	+	?	?	-	+
Sun et al., 2022[13]	+	+	?	?	-	+
Suzuki et al., 2021[14]	-	+	+	?	-	+
Smith et al., 2020[15]	+	+	+	?	+	+
Teymoori et al., 2020[16]	+	+	-	?	+	+

+ Low Risk of Bias
- indicates High Risk of Bias
? Unknown Risk of Bias

Discussion

Neuropathic pain caused by nerve damage, infection, or disease is often severe and chronic. Patients with chronic pain may experience abnormal sensations such as allodynia and hyperalgesia as well as emotional disturbances such as depression and anxiety[17]. It is noteworthy that the cross-sectional studies included in this review showed an association between depression and chronic neuropathic pain. Sachau et al.[12] found a significant association between depression and neuropathic pain, demonstrating the impact of pain phenotypes on mental health. Similarly, Smith et al.[15] identified the relationship between depressive symptoms and various types of neuropathic pain, underscoring the need for targeted interventions for pain and mental illness.

Additionally, Teymoori et al.[16] reported an increased risk of depression and anxiety over time in patients with traumatic brain injury, demonstrating the long-term impact of neurological disease

on the clinical outcomes of the brain. These long-term findings highlight the importance of ongoing care and quality care to address the long-term effects of neurological disease. A bibliometric analysis was conducted on the studies related to neurological pain and depression from 2000 to 2020. The study included 915 articles from the WoS database. Judging by the emerging terms, neuroinflammation, hippocampus, safety and control are hot international research topics in this field. From 2000 to 2020, there was an increase in the number of NP reports of depression or anxiety[18]. While Suzuki et al.[14] and Sun et al.[13] describe the complicated subject of neurological disorders, neuropathic pain, and depression and their integrated management in medicine, the fact remains that it still must be tackled on a large scale. According to the researchers cited in the study, the shared neurobiological mechanisms of neuropathic pain and depression are working based on these pathways. They are likely to bring about both disorders. They highlight the need for the generalized approach focused on targeting central sensitization for success in referring pain-conditioned diseases that do not improve with treatment.

On the other hand, the same article underscores the significance of the rising incidence of depression among patients with neurological disorders by emphasizing the need for attention as well as adequate screening and intervention within non-psychiatric hospital settings. These findings, therefore, advocate for the introduction of the PHQ-9 as the appropriate tool for the assessment of depression severity, whereas the role of age and gender is worthwhile to include in further research. On top of the obvious, joblessness became another threat factor for the population of depression. Perhaps the studies cited here provide all elements of the nuanced interplay between psychiatric conditions, mood disturbance, and sociodemographic influence, which then demands continuous research to provide further improvement in clinical practice.

The results of this review highlight the importance of the relationship between neuropathic pain and depression and draw attention to the relationship between physical and mental health. Clinical studies consistently demonstrate an association between neuropathic pain and depressive symptoms, highlighting the need for assessment and management strategies that address both physical and mental aspects of care. People with neuropathic pain often experience symptoms of depression, anxiety, and social isolation; this can exacerbate pain and lead to a cycle of dysfunction and disability.

Conclusion

The synthesis of findings from diverse studies underscores the bidirectional relationship between neuropathic pain and depression, emphasizing the need for integrated approaches to pain management and mental health care. Future research should focus on elucidating the underlying mechanisms linking neuropathic pain and depressive symptoms and developing tailored interventions to improve outcomes for individuals with co-occurring neurological and psychiatric conditions.

Authors Contribution

Jehangir S: Conception, design and data acquisition.

Atif S: Data acquisition and analysis.

Sajid A: Manuscript Writing.

Khalid SS: Manuscript Writing, Revising the draft.

Declaration of Interest

None.

Funding Sources

None.

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