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Mini Review

Recognizing and Treating Co-Morbid Pain and Depression

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ABSTRACT

Chronic pain and depression have a reciprocal relationship where each one increases the risk for and impacts the experience of the other. Because these conditions co-occur at a high rate, with depression often going unrecognized, more focus on diagnosing and treating the entire constellation of symptoms that pain and depression patients experience is warranted. The shared neural mechanisms of chronic pain and depression offer opportunities for treatment, though evidence suggests that the most effective and long-lasting treatments will combine pharmacological interventions and psychotherapy. There will likely not be a one-size-fits-all treatment approach for comorbid pain and depression patients, but clinicians should base their recommendations on clinical evaluations of patients that assess both pain and depression.

Keywords: Scapular dyskinesis; Overhead sports; Volleyball; Psychotherapy

INTRODUCTION

Depression and chronic pain are two of the world's leading causes of disability [1-3]. According to the World Health Organization (WHO), more than 264 million people suffer from depression [3]. While rates of chronic pain vary across the globe, 2019 data from the U.S. Centers for Disease Control and Prevention (CDC) show that more than 1 in 5 people in the U.S. suffer from the condition [4]. Other countries display even higher chronic pain rates [5].

Depression and chronic pain tend to be viewed as separate conditions and treated accordingly. Critically, though, accumulating evidence suggests that depression and chronic pain not only co-occur at high rates, but that depression increases pain severity and that chronic pain leads to depression. Further, it is becoming clear that each disorder can exacerbate the other.

Data reveal that more than 85% of those with chronic pain also experience severe depression and that depression is often pain-induced [6-10]. In addition, chronic pain and depression appear to mutually promote the progression of each of the disorders [11]. The clinical management of depression and chronic pain should thus be adjusted in light of this evidence of the high levels of co-occurrence of these conditions and the risks that these conditions pose for the development or exacerbation of one another. Critically, both pharmacotherapy and psychotherapy should be appropriately deployed to address chronic pain and depression.

THERE IS A VICIOUS CYCLE WHERE PAIN BEGETS DEPRESSION AND VICE VERSA

We have evolved to perceive pain for good reason; pain serves to protect us from dangerous, potentially life-threatening situations. For instance, acute pain activates spinal reflexes that help us to physically withdraw from potentially damaging stimuli and retreat from danger [12]. An analogous argument could be posed for the function of emotional pain. Feelings of sadness or frustration may teach us to avoid unhealthy circumstances and learn how to solve problems.

Despite its potential utility, pain that continues beyond what is biologically useful causes unnecessary suffering. Acute pain that is experienced at a heightened level and chronic pain, which serves little practical purpose, are maladaptive and should be

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prevented or treated. Importantly, this unnecessary pain carries not only a physical burden but a psychological one as well.

As recognized by the International Association for the Study of Pain, pain is not only unpleasant from a sensory perspective but also from an emotional one [13]. Pain is thus to some degree a subjective experience that does not depend entirely on the nature or degree of the relevant stimuli. It is therefore perhaps not surprising that people's subjective experience with chronic pain is different if they suffer from clinical depression [14].

Those with depression are more likely to perceive pain as more severe than those without depression [15]. Even when there is no physiological justification for different pain levels, people with depression are more likely to report higher levels of pain than those without depression [16]. The neural mechanisms that prime people to perceive emotional pain more severely may also prime people to perceive physical pain more severely.

What is particularly troubling is that not only does depression increase sensitivity to both psychological and physical pain, but chronic pain can also lead to depression in cases where depression did not precede the pain [17,18].This reciprocal relationship between chronic pain and depression has led to significant research into the neural mechanisms linking the disorders.

Depression and chronic pain share overlapping brain mechanisms

Given the limited space and computational capacity of the brain, it is reasonable that the processing of different types of pain-e.g. physical and psychological-may employ redundant physiological mechanisms. Chronic pain or pain that lasts for more than 3 months persistently or intermittently and depression appear to be associated with common neurological changes that may help to explain why these conditions are often observed together [18,19].

Hypothalamic-Pituitary Adrenal (HPA) dysfunction induced by chronic stress, for instance, could help to explain the link between chronic pain and depression [12]. Common sites of action for chronic pain and depression include the relevant areas such as brainstem nuclei, the limbic system, and the somatosensory cortices.

In addition to changes in functional anatomy, chronic pain and depression share some signaling changes within the brain as well. For example, Brain-Derived Neurotrophic Factor (BDNF) is implicated in both chronic pain and depression. It contributes to the experience of pain by, for instance, regulating pain hypersensitivity [20,21]. Compared to people without depression, people with depression have lower BDNF blood concentration and lower levels of BDNF expression in areas of the brain associated with depression, including the prefrontal cortex and hippocampus [22-24].

Certain neurotransmitters appear to play a role in both chronic pain and depression as well. Examples are monoamine neurotransmitters such as serotonin, dopamine, and norepinephrine [18,25]. Midbrain dopamine activity may be particularly relevant in chronic pain and depression, as it contributes significantly to forebrain functions that are important in both depression and pain perception [18]. Another neurotransmitter, glutamate, is a main excitatory neurotransmitter of the nervous system that, along with its receptors, N-Methyl-D-Aspartic acid (NMDA) receptor and α-Amino-3-Hydroxy-5-Methyl-4-isoxazolepropionic Acid (AMPA), have been shown to be involved in both depression and chronic pain [26-28].

Dysfunctional inflammatory processes and specific inflammatory signals in the brain may also contribute to both chronic pain and depression [29]. Specifically, these signals can lead to depression by altering neuroendocrine function and neurotransmitter metabolism [30]. Consistent with this role of inflammation in depression, studies have shown 45% of patients who receive systemic treatments of INF-α for conditions like hepatitis C or malignant melanoma are diagnosed with major depressive disorder [31-33]. Pains that result from inflammation are more strongly linked to depression than other forms of pain [18].

PAIN PATIENTS SHOULD BE ASSESSED FOR DEPRESSION, AND DEPRESSED PATIENTS SHOULD BE ASSESSED FOR PAIN

Data from a World Health Organization study have shown that nearly 70% of patients across 14 countries have reported somatic symptoms as the only reason for their visit, despite displaying depression [34]. There is thus concern about depression going undiagnosed in patients with comorbid pain and depression [35]. Troublingly, patients with chronic pain have increased levels of suicidal thoughts compared to those who do not have chronic pain, and if these thoughts and other signs of depression are not captured clinically, treatment strategies may be suboptimal [35,36]. The specific types of pain symptoms that are commonly associated with depression include joint pain, back pain, headache, limb pain, and gastrointestinal pain [35]. Generally the more severe the physical pain, the more severe the depression [35]. Clinicians should therefore take into account the severity of both physical and psychological pain when providing treatment recommendations [37].

Similarly, it is becoming increasingly recognized that physical symptoms have perhaps been unjustifiably ignored in depression assessments and potentially interpreted as signs of somatic illness rather than related to the depression [35]. Pain relief is often not included in treatment goals for the same reason. However, even when acute emotional symptoms of depression have abated, persistent physical symptoms may increase the likelihood of depression relapse. Indeed, depression patients who have residual symptoms that persist following treatment are 3 times more likely to relapse than those without residual symptoms [38]. Experts have thus argued that therapy should be continued until patients are asymptomatic or lacking signs of both physical and emotional distress [35].

SUCCESSFUL TREATMENT OF CHRONIC PAIN AND DEPRESSION LIKELY INCLUDES A COMBINATION OF PHARMACOTHERAPY AND PSYCHOTHERAPY

Meta-analysis results on the effects of antidepressants on pain have shown that these drugs are more than 74% effective than placebo in providing pain relief in people who suffer from chronic pain [39]. These data point to the potential for antidepressants to influence overlapping mechanisms of chronic pain and depression and effectively address symptoms of each condition. One potential neurological mechanism by which pain and depression co-occur is an imbalance in serotonin and norepinephrine. In cases where this imbalance contributes to the two disorders, antidepressants that inhibit the reuptake of these neurotransmitters-such as venlafaxine and duloxetine-may be more likely than other types of antidepressants to alleviate pain [35,40].

Research into serotonin-selective drugs has shown rather than targeting 5-HT1A receptors, activating 5-HT heteroreceptors appears more effective for simultaneously treating chronic pain and depression [41]. Tricyclic antidepressants, however, appear to provide more effective pain relief than is provided by serotonin-selective drugs, suggesting that perhaps these antidepressants achieve benefits for depression and pain independently [42].

In addition to pharmacotherapy, psychotherapy is often recommended for patients with depression and patients with chronic pain [43,44]. While much of the relevant literature focuses on the efficacy of psychotherapy on either chronic pain or depression alone, there are also data that support the value of psychotherapy in patients with comorbid chronic pain and depression [45,46].

The best type of psychotherapy for chronic pain may differ based on the nature of the pain or the psychology of the patient, but these therapies can complement other therapies to address chronic pain and depression [43]. There is a growing body of evidence, for instance, that Cognitive Behavioral Therapy (CBT) can help to alleviate both chronic pain and depression [47-49]. As with other forms of psychotherapy, cognitive behavioral strategies also show promise for treating patients experiencing chronic pain and depression simultaneously [46].

DISCUSSION

Comorbid chronic pain and depression is likely an underappreciated contributor to long-term disability and suffering. Though antidepressants represent a gold standard for depression therapy, treating chronic pain is arguably more difficult because of the interdisciplinary requirements and spectrum of therapeutic options which may include pharmacotherapy, psychotherapy, and even neurosurgery [12]. Recognizing the potential role of depression in chronic pain offers an opportunity to more comprehensively address chronic pain through strategies that treat depression.

Specifically, to effectively reduce disability associated with chronic pain, one must address depression with the necessary tools, including pharmacological intervention, as well as psychiatric and psychological intervention [50-52]. In the case of chronic pain, nonpharmacological therapies are invaluable [53,54]. Though they can serve as standalone therapies, these therapies are often used to complement pharmacological interventions for chronic pain, and the treatment plan for each patient should be customized based on the patient's specific pain and psychological condition.

CONCLUSION

In cases where depression is readily diagnosed, persistent chronic pain enhances the risk for remission. It is therefore critical that providers caring for those with depression assess not only emotional well-being but also physical comfort and the presence of pain. Even in cases where antidepressants are highly effective, pairing the therapy with strategies to overcome pain may provide a more complete and long-term solution for the patient.

Given that different providers may care for patients with depression and patients with chronic pain, there is a significant need for collaborative efforts that enable healthcare providers to recognize the presence and appreciate the implications of a comorbid condition in these patients. With a growing understanding of the co-occurrence of chronic pain and depression and the risks associated with leaving one of these conditions unaddressed from a therapeutic standpoint, we will be better equipped to improve quality of life and reduce the burden of disease for patients with chronic pain and depression.

REFERENCES

1. Vos T, Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: A systematic analysis for the global burden of disease study 2016. Lancet. 2017;390(10100):1211-1259.
2. Mills SE, Nicolson KP, Smith BH. Chronic pain: A review of its epidemiology and associated factors in population-based studies. Br J Anaesth. 2019;123(2):e273-283.
3. Depression. World Health Organization. 2020.
4. Zelaya CE, Dahlhamer JM, Lucas JW, Connor EM. Key findings Data from the National Health Interview Survey. National Center for Health Statistics. 2007.
5. Souza JB, Grossmann E, Perissinotti DM, Junior JOO, Fonseca PR, Posso ID. Prevalence of chronic pain, treatments, perception, and interference on life activities: Brazilian population-based survey. Pain Res Manag. 2017;2017:4643830.
6. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: A literature review. Arch Intern Med. 2003;163(20): 2433-2445.
7. Williams LS, Jones WJ, Shen J, Robinson RL, Weinberger M, Kroenke K. Prevalence and impact of depression and pain in neurology outpatients. J Neurol Neurosurg Psychiatry. 2003;74(11): 1587-1589.
8. Agüera-Ortiz L, Failde I, Mico JA, Cervilla J, López-Ibor JJ. Pain as a symptom of depression: Prevalence and clinical correlates in patients attending psychiatric clinics. J Affect Dis. 2011;130(1-2):106-112.

9. Pyo PL, Kuang-Peng HH, Tang CS. Frequency of painful physical symptoms with major depressive disorder in Asia: Relationship with disease severity and quality of life. J Clin Psychiatry. 2008;69(1):0-0.
10. Knorring VL, Perris C, Oreland L, Eisemann M, Eriksson U, Perris H. Pain as a symptom in depressive disorders and its relationship to platelet monoamine oxidase activity. J Neural Transm. 1984;60(1):1-9.
11. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS. Chronic pain-associated depression: Antecedent or consequence of chronic pain? A review. Clin J Pain. 1997;13(2):116-137.
12. Blackburn-Munro G, Blackburn-Munro RE. Chronic pain, chronic stress and depression: Coincidence or consequence?. J Neuroendocrinol. 2001;13(12):1009-1023.
13. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. Pain Suppl. 1986;3:S1-S226.
14. Magni G. On the relationship between chronic pain and depression when there is no organic lesion. Pain. 1987;31(1):1-21.
15. Michaelides A, Zis P. Depression, anxiety and acute pain: links and management challenges. Postgraduate medicine. 2019;131(7):438-444.
16. Wilson KG, Mikail SF, Joyce LD, Minns JE. Alternative diagnostic criteria for major depressive disorder in patients with chronic pain. Pain. 2001;91(3):227-234.
17. Conejero I, Olié E, Calati R, Ducasse D, Courtet P. Psychological pain, depression, and suicide: Recent evidences and future directions. Curr Psychiatry Rep. 2018;20(5):1-9.
18. Sheng J, Liu S, Wang Y, Cui R, Zhang X. The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain. Neural Plast. 2017;27829-001.
19. Doan L, Manders T, Wang J. Neuroplasticity underlying the comorbidity of pain and depression. Neural Plast. 2015;504691.
20. Garraway SM, Huie JR. Spinal plasticity and behavior: BDNF-induced neuromodulation in uninjured and injured spinal cord. Neural Plast. 2016;9857201.
21. Yajima Y, Narita M, Usui A, Kaneko C, Miyatake M, Narita M, et al. Direct evidence for the involvement of brain-derived neurotrophic factor in the development of a neuropathic pain-like state in mice. J Neuro Chem. 2005;93(3):584-594.
22. Villanueva R. Neurobiology of major depressive disorder. Neural Plast. 2013;873278.
23. Bocchio-Chiavetto L, Bagnardi V, Zanardini R, Molteni R, Nielsen GM, Placentino A, et al. Serum and plasma BDNF levels in major depression: A replication study and meta-analyses. World J Biol Psychiatry. 2010;11(6):763-773.
24. Krishnan V, Nestler EJ. The molecular neurobiology of depression. Nature. 2008;455(7215):894-902.
25. Basbaum AI, Fields HL. Endogenous pain control mechanisms: review and hypothesis. Ann Neurol. 1978;4(5):451-462.
26. Paoletti P, Bellone C, Zhou Q. NMDA receptor subunit diversity: Impact on receptor properties, synaptic plasticity and disease. Nat Rev Neurosci. 2013;14(6):383-400.
27. Zanos P, Moaddel R, Morris PJ, Georgiou P, Fischell J, Elmer GI, et al. NMDAR inhibition-independent antidepressant actions of ketamine metabolites. Nature. 2016;533(7604):481-486.
28. Yao L, Zhou Q. Enhancing NMDA receptor function: Recent progress on allosteric modulators. Neural Plast. 2017; 2875904.
29. Huang WJ, Chen WW, Zhang X. Endocannabinoid system: Role in depression, reward and pain control. Mol Med Rep. 2016;14(4):2899-2903.
30. Walker AK, Kavelaars A, Heijnen CJ, Dantzer R. Neuroinflammation and comorbidity of pain and depression. Pharmacol Rev. 2014;66(1):80-101.
31. Musselman DL, Lawson DH, Gumnick JF, Manatunga AK, Penna S, Goodkin RS, et al. Paroxetine for the prevention of depression induced by high-dose interferon alfa. N Engl J Med. 2001;344(13):961-966.
32. Capuron L, Neurauter G, Musselman DL, Lawson DH, Nemeroff CB, Fuchs D, et al. Interferon-alpha–induced changes in tryptophan metabolism: Relationship to depression and paroxetine treatment. Biol Psychiatry. 2003;54(9):906-914.
33. Capuron L, Ravaud A, Dantzer R. Early depressive symptoms in cancer patients receiving interleukin 2 and/or interferon alfa-2b therapy. J Clin Oncol. 2000;18(10):2143-2151.
34. Simon GE, VonKorff M, Piccinelli M, Fullerton C, Ormel J. An international study of the relation between somatic symptoms and depression. N Engl J Med. 1999;341(18):1329-1335.
35. Trivedi MH. The link between depression and physical symptoms. Prim Care Companion J Clin Psychiatry. 2004;6(suppl 1):12.
36. Fishbain DA. The association of chronic pain and suicide. Clin Neuropsychiatry. 1999;4(3):221-227.
37. Vietri J, Otsubo T, Montgomery W, Tsuji T, Harada E. Association between pain severity, depression severity, and use of health care services in Japan: Results of a nationwide survey. Neuropsychiatr Dis Treat. 2015;11:675-683.
38. Judd LL, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, et al. Major depressive disorder: A prospective study of residual subthreshold depressive symptoms as predictor of rapid relapse. J Affect Disord. 1998;50(2-3):97-108.
39. Onghena P, Houdenhove VB. Antidepressant-induced analgesia in chronic non-malignant pain: A meta-analysis of 39 placebo-controlled studies. Pain. 1992;49(2):205-219.
40. Stahl SM. Does depression hurt?. J Clin Psychiatry. 2002;63(4):273-304.
41. Haleem DJ. Targeting Serotonin1A receptors for treating chronic pain and depression. Curr Neuropharmacol. 2019;17(12):1098-1108.
42. Smith AJ. The analgesic effects of selective serotonin reuptake inhibitors. J Psychopharmacol. 1998;12(4):407-413.
43. Sturgeon JA. Psychological therapies for the management of chronic pain. Psychol Res Behav Manag. 2014;7:115-124.
44. Munder T, Flückiger C, Leichsenring F, Abbass AA, Hilsenroth MJ, Luyten P, et al. Is psychotherapy effective? A re-analysis of treatments for depression. Epidemiol Psychiatr Sci. 2019;28(3):268-274.
45. Poleshuck EL, Talbot NE, Zlotnick C, Gamble SA, Liu X, Tu X, et al. An interpersonal psychotherapy approach for comorbid depression and chronic pain. J Nerv Ment Dis. 2010;198(8):597-600.
46. Barrett K, Chang YP. Behavioral interventions targeting chronic pain, depression, and substance use disorder in primary care. J Nurs Scholarsh. 2016;48(4):345-353.
47. Ehde DM, Dillworth TM, Turner JA. Cognitive-behavioral therapy for individuals with chronic pain: efficacy, innovations, and directions for research. Am Psychol. 2014;69(2):153-166.
48. Gautam M, Tripathi A, Deshmukh D, Gaur M. Cognitive Behavioral Therapy for Depression. Indian J Psychiatry. 2020;62(Suppl 2):S223.
49. Gautam S, Jain A, Gautam M, Vahia VN, Grover S. Clinical practice guidelines for the management of depression. Indian J Psychiatry. 2017;59(Suppl 1):S34.
50. Schwarze M, Häuser W, Schmutzer G, Brähler E, Beckmann NA, Schiltenwolf M. Obesity, depression and hip pain. Musculoskelet Care. 2019;17(1):126-132.
51. Patsalos O, Keeler J, Schmidt U, Penninx BWJH, Young AH, Himmerich H. Diet, Obesity, and Depression: A Systematic Review. J Pers Med. 2021;11(3):176.

52. Schuch FB, Vancampfort D, Richards J, Rosenbaum S, Ward PB, Stubbs B. Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. J Psychiatr Res. 2016;77:42-51.

53. Borisovskaya A, Chmelik E, Karnik A. Exercise and Chronic Pain. In: Xiao J (eds) Physical Exercise for Human Health. Advances in Experimental Medicine and Biology. 2020;1228: pp 233-253.

54. Chang KL, Fillingim R, Hurley RW, Schmidt S. Chronic pain management: Nonpharmacological therapies for chronic pain. FP Essent. 2015;432:21-26.