Pain Mechanism Classification Clinical Pearl
Part 4: Nociplastic Pain

Introduction

This is the fourth and final Clinical Pearl in our series on the pain mechanism-based approach to physical therapy management of individuals with pain (Part 1, Part 2, Part 3). It has been suggested that using an assessment and treatment framework that incorporates the identification of pain mechanisms (nociceptive, neuropathic, and nociplastic) may enable use of focused interventions that affect the underlying mechanism(s) and optimize patient outcomes.[1] This Pearl will focus on nociplastic pain, which is defined by the International Association for the Study of Pain (IASP) as "pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain." A summary of clinically relevant examination and treatment concepts will be discussed.

Examination

Features of nociplastic pain can be assessed through subjective and physical examination. An underlying neurophysiological process that is common in a nociplastic pain presentation is central sensitization. Smart et al. developed and tested a cluster of signs and symptoms that would distinguish central sensitization from nociceptive and neuropathic pain mechanisms.[2] Since the publication of this work, there has been a shift towards using the term "nociplastic pain" instead of "central sensitization" since central sensitization is only one feature of a nociplastic pain state, but to be consistent with Smart et al.'s descriptions we will use "central sensitization" here. Central sensitization is a neurophysiologic phenomenon that is not directly measurable clinically. This cluster included four signs and symptoms that suggest the presence of central sensitization: (1) Pain disproportionate to the nature and extent of injury or pathology, (2) disproportionate, non-mechanical, unpredictable pattern of pain provocation in response to multiple/non-specific aggravating/easing factors, (3) strong association with maladaptive psychosocial factors (negative emotions, poor self-efficacy, maladaptive beliefs and pain behaviors, and altered family/work/social life), and (4) diffuse/non-anatomic areas of pain/tenderness on palpation.[2] If a patient presents with all four of these factors, there is a 486x increased likelihood of the presence of central sensitization.[2] Again, these factors are signs of central sensitization, not nociplastic pain itself. Therefore, they are only part of the clinician's assessment of a nociplastic pain presentation. Further work has suggested other comorbidities

may also be correlated with nociplastic pain including sensitivity to sound, light, and/or odors, sleep disturbance, fatigue, and cognitive problems (focus, attention, and memory disturbance).[3] A thorough subjective history can determine the presence or absence of these factors.

As previously discussed, there is a strong association of nociplastic pain with maladaptive beliefs about pain and psychosocial factors. There are many validated self-report questionnaires that can help to determine the presence or absence of such features. A full discussion of these questionnaires is not within the scope of this Clinical Pearl. A good starting point for the clinician is to use the OSPRO Yellow Flag (OSPRO-YF) tool, which is a screening tool used to assess for many possible psychological factors that may correlate with nociplastic pain.[4] The Academy of Orthopedic Physical Therapy offers an online tool to analyze the results of this questionnaire (https://www.orthopt.org/yf/) and the clinician may then choose the most relevant full form questionnaires to apply to further explore psychological factors that may be present in the individual they are assessing. These questionnaires are not diagnostic of a nociplastic pain state, but rather may give the clinician insight on relevant patient beliefs and psychological states that may affect treatment and outcomes.

While all three pain mechanisms may be involved in a painful condition, the identification of a dominant mechanism can assist the clinician in sound clinical reasoning regarding which interventions may have the most positive impact on the patient. If nociplastic pain is suspected as the dominant pain mechanism following the subjective examination, then the physical examination should be tailored to identify the presence of physical signs that would support or refute this hypothesis. This should incorporate the identification of the relative contribution of nociceptive and neuropathic pain mechanisms. The reader is referred to the previous three Clinical Pearls in this series for further information on those pain mechanisms. Physical examination that may identify central sensitization is a component of determining if nociplastic pain is a dominant pain mechanism.

Central sensitization is not directly measurable and must be inferred from tests such as quantitative sensory testing.[5] These testing modalities are expensive and not widely available in the clinic and therefore, there are clinically-feasible tests that have been suggested.[5] Such testing is crude but may be useful to identify certain features of central sensitization. For example, cold/heat hyperalgesia may be identified using a metal object calibrated to 20°C (cold hyperalgesia) and 40°C (heat allodynia).[3] Dynamic mechanical allodynia can be assessed by the presence of pain with repeated light touch via a cotton wool tip or soft brush.[5] A clinically feasible test for static mechanical allodynia is the use of nailbed blanching pressure (approximately 4 kg) to assess for pain, the presence of which would be considered pressure allodynia.[5] Alternatively, a clinician can use the Central Sensitization Inventory questionnaire to assess for central sensitization, with a cutoff score of 40/100 or higher indicating the presence of central sensitization.[6,7] Beyond specific testing for central sensitization, the use of a “big picture” assessment of functional movements (e.g. walking, transfers, squats, lifts) is useful for keeping the focus of rehabilitation on function rather than on specific tissue capabilities or pathologies. During such testing, you may find that the individual reports pain out of proportion

to the aggravating factor or movement. Such testing may be useful to establish patient-focused functional goals.

Treatment

Individuals with nociplastic pain may benefit from treatment centered around movement. One approach to movement is a structured exercise program. The effect of exercise on pain intensity is uncertain, but it has positive effects on function and psychological factors for individuals with nociplastic pain.[8] There are many proposed mechanisms for how exercise affects these constructs.[1] There is a lack of evidence to suggest a superior modality or dose of exercise for treating nociplastic pain but guidelines have been suggested.[9] Other forms of movement that may be used therapeutically are graded activity and graded exposure. These movement therapies have been shown to be equally as effective as exercise at improving pain and function in individuals with persistent low back pain.[10] Clinically, this may offer an alternative to traditional exercise programs for individuals who have low self-efficacy for exercise.

Another key component of treatment for individuals with nociplastic pain is psychologically targeted interventions to address any identified maladaptive pain beliefs or psychological states. Cognitive behavioral therapy (CBT), acceptance and commitment therapy (ACT), and pain neuroscience education (PNE) have been shown to have positive impacts on pain, function, and associated psychological factors for individuals with nociplastic pain.[11-16] A key factor in the effectiveness of psychologically targeted interventions may be the patient's readiness to change their beliefs about their pain. Motivational interviewing may be an effective way to assess the patient's stage of readiness to change using the trans-theoretical model.[17] Determining this may help to optimize the style and dose of intervention.

Manual therapy is a common component of treatment for individuals with nociplastic pain. When manual therapy is applied, the mechanical stimulus sets off a chain of neurophysiological effects that can modulate pain at the level of the central nervous system.[18] Included in this are changes to areas of the brain and spinal cord that are responsible for the modulation of pain (see Bialosky et al. for further details).[18] Furthermore, individuals with nociplastic pain tend to exhibit changes in the primary sensory cortex including impairments with laterality judgements and body schema.[19] It has been suggested that utilizing manual therapy can have positive effects on these impairments and "sharpen" the sensory homunculus.[19] Utilizing PNE to help explain these mechanisms of manual therapy and how this treatment may help to reduce pain may enhance patient expectations of improvement, which has been shown to subsequently improve the results of treatment.[19]

There is emerging focus on the modification of lifestyle factors as adjunct treatment alongside traditional physical therapy interventions. These include sleep hygiene, nutrition, and stress reduction among others. There is a known, bidirectional relationship between pain and sleep.[20] There is evidence that adding a cognitive behavioral therapy (CBT) based approach for addressing insomnia related to chronic low back to physical therapy management provides greater reductions in pain.[20] Nutrition also has a bidirectional relationship with pain.[21] Many

types of diets focused on inflammation reduction have been shown to be beneficial for pain reduction, weight management, and prevention of comorbid diseases for individuals with pain.[21] Lastly, stress reduction may be another important lifestyle factor that can be beneficial for individuals with nociplastic pain. One treatment that is feasible for physical therapists to implement and for patients to use for self-management is mindfulness-based stress reduction. There is evidence that this reduces pain and improves function and quality of life for individuals with persistent pain.[22,23]

Summary

- Examination
    - There are key subjective findings that suggest nociplastic pain is a dominant pain mechanism
    - The OSPRO-YF tool can be used to screen for, and determine need for further assessment of, related psychological factors
    - There are clinically feasible tests that serve as a proxy for quantitative sensory testing and a cutoff score of 40/100 on the CSI can be used to screen for the presence of central sensitization
    - Keeping a focus of your movement examination on functional movements helps to de-emphasize pathoanatomical beliefs and set functional goals
- Treatment
    - Movement (exercise and/or graded activity/exposure) and psychologically informed targeted interventions are key interventions for all patients
    - Using motivational interviewing to assess readiness to change beliefs about pain can be helpful in tailoring the delivery of psychologically informed interventions
    - Manual therapy has neurophysiologic effects that can be positive for individuals with nociplastic pain, especially when given in the context of PNE
    - Lifestyle modification (sleep, nutrition, and stress reduction) treatments are potential adjunct treatments and can be feasibly delivered by physical therapists

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References

1) Chimenti RL, Frey-Law LA, Sluka KA. A Mechanism-Based Approach to Physical Therapist Management of Pain. Phys Ther. 2018;98(5):302-314. doi:10.1093/ptj/pzy030
2) Smart KM, Blake C, Staines A, Doody C. The Discriminative validity of "nociceptive," "peripheral neuropathic," and "central sensitization" as mechanisms-based classifications of musculoskeletal pain. Clin J Pain. 2011;27(8):655-663. doi:10.1097/AJP.0b013e318215f16a

3) Kosek E, Clauw D, Nijs J, et al. Chronic nociplastic pain affecting the musculoskeletal system: clinical criteria and grading system. Pain. 2021;162(11):2629-2634. doi:10.1097/j.pain.0000000000002324
4) Lentz TA, Beneciuk JM, Bialosky JE, et al. Development of a Yellow Flag Assessment Tool for Orthopaedic Physical Therapists: Results From the Optimal Screening for Prediction of Referral and Outcome (OSPRO) Cohort [published correction appears in J Orthop Sports Phys Ther. 2016 Sep;46(9):813]. J Orthop Sports Phys Ther. 2016;46(5):327-343. doi:10.2519/jospt.2016.6487
5) van Griensven H, Schmid A, Trendafilova T, Low M. Central Sensitization in Musculoskeletal Pain: Lost in Translation?. J Orthop Sports Phys Ther. 2020;50(11):592-596. doi:10.2519/jospt.2020.0610
6) Neblett R, Cohen H, Choi Y, et al. The Central Sensitization Inventory (CSI): establishing clinically significant values for identifying central sensitivity syndromes in an outpatient chronic pain sample. J Pain. 2013;14(5):438-445. doi:10.1016/j.jpain.2012.11.012
7) Neblett R, Hartzell MM, Cohen H, et al. Ability of the central sensitization inventory to identify central sensitivity syndromes in an outpatient chronic pain sample. Clin J Pain. 2015;31(4):323-332. doi:10.1097/AJP.0000000000000113
8) Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. Cochrane Database Syst Rev. 2017;4(4):CD011279. Published 2017 Apr 24. doi:10.1002/14651858.CD011279.pub3
9) Booth J, Moseley GL, Schiltenwolf M, Cashin A, Davies M, Hübscher M. Exercise for chronic musculoskeletal pain: A biopsychosocial approach. Musculoskeletal Care. 2017;15(4):413-421. doi:10.1002/msc.1191
10) López-de-Uralde-Villanueva I, Muñoz-García D, Gil-Martínez A, et al. A Systematic Review and Meta-Analysis on the Effectiveness of Graded Activity and Graded Exposure for Chronic Nonspecific Low Back Pain. Pain Med. 2016;17(1):172-188. doi:10.1111/pme.12882
11) Louw A, Zimney K, Puentedura EJ, Diener I. The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature. Physiother Theory Pract. 2016;32(5):332-355. doi:10.1080/09593985.2016.1194646
12) Bonatesta L, Ruiz-Cárdenas JD, Fernández-Azorín L, Rodríguez-Juan JJ. Pain Science Education Plus Exercise Therapy in Chronic Nonspecific Spinal Pain: A Systematic Review and Meta-analyses of Randomized Clinical Trials. J Pain. 2022;23(4):535-546. doi:10.1016/j.jpain.2021.09.006
13) Siddall B, Ram A, Jones MD, Booth J, Perriman D, Summers SJ. Short-term impact of combining pain neuroscience education with exercise for chronic musculoskeletal pain: a systematic review and meta-analysis. Pain. 2022;163(1):e20-e30. doi:10.1097/j.pain.0000000000002308
14) Wood L, Hendrick PA. A systematic review and meta-analysis of pain neuroscience education for chronic low back pain: Short-and long-term outcomes of pain and disability. Eur J Pain. 2019;23(2):234-249. doi:10.1002/ejp.1314
15) Williams ACC, Fisher E, Hearn L, Eccleston C. Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst

Rev. 2020;8(8):CD007407. Published 2020 Aug 12. doi:10.1002/14651858.CD007407.pub4
16) Hughes LS, Clark J, Colclough JA, Dale E, McMillan D. Acceptance and Commitment Therapy (ACT) for Chronic Pain: A Systematic Review and Meta-Analyses. Clin J Pain. 2017;33(6):552-568. doi:10.1097/AJP.0000000000000425
17) Nijs J, Wijma AJ, Willaert W, et al. Integrating Motivational Interviewing in Pain Neuroscience Education for People With Chronic Pain: A Practical Guide for Clinicians. Phys Ther. 2020;100(5):846-859. doi:10.1093/ptj/pzaa021
18) Bialosky JE, Beneciuk JM, Bishop MD, et al. Unraveling the Mechanisms of Manual Therapy: Modeling an Approach. *J Orthop Sports Phys Ther*. 2018;48(1):8-18. doi:10.2519/jospt.2018.7476
19) Puentedura EJ, Flynn T. Combining manual therapy with pain neuroscience education in the treatment of chronic low back pain: A narrative review of the literature. Physiother Theory Pract. 2016;32(5):408-414. doi:10.1080/09593985.2016.1194663
20) Van Looveren E, Meeus M, Cagnie B, et al. Combining Cognitive Behavioral Therapy for Insomnia and Chronic Spinal Pain Within Physical Therapy: A Practical Guide for the Implementation of an Integrated Approach. Phys Ther. 2022;102(8):pzac075. doi:10.1093/ptj/pzac075
21) Tatta J, Nijs J, Elma Ö, Malfliet A, Magnusson D. The Critical Role of Nutrition Care to Improve Pain Management: A Global Call to Action for Physical Therapist Practice. Phys Ther. 2022;102(4):pzab296. doi:10.1093/ptj/pzab296
22) Pardos-Gascón EM, Narambuena L, Leal-Costa C, van-der Hofstadt-Román CJ. Differential efficacy between cognitive-behavioral therapy and mindfulness-based therapies for chronic pain: Systematic review. Int J Clin Health Psychol. 2021;21(1):100197. doi:10.1016/j.ijchp.2020.08.001
23) Petrucci G, Papalia GF, Russo F, et al. Psychological Approaches for the Integrative Care of Chronic Low Back Pain: A Systematic Review and Metanalysis. Int J Environ Res Public Health. 2021;19(1):60. Published 2021 Dec 22. doi:10.3390/ijerph19010060