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Targeting Central Sensitization in Patients with Chronic Musculoskeletal Conditions

Tanvi Patole[1], Sunil Rajpal[2].
Assistant Professor, K J Somaiya College of Physiotherapy
Deputy Head, Department of Rehab & Sports Medicine Sir HN Reliance Foundation Hospital, Mumbai
Corresponding Author: Tanvi Patole

Abstract: *Pain is the main presenting symptom in musculoskeletal conditions. The understanding of unexplained chronic pain disorders has increased substantially. The majority of cases of chronic musculoskeletal pain are characterized by abnormal pain processing mechanisms. There is a possibility that, the pain experience might not necessarily reflect the consistent relationship between pathology and pain. Therefore, it is important to find out distal or peripheral mechanisms to treat patients effectively with the help of physiotherapy.*

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I. Theories Of Variations In Pain Perception And Reporting

Pain is the main presenting symptom in musculoskeletal conditions. International Association for the Study of Pain defines Pain as follows, "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [1]." Considerable importance is given to the patient's pain reporting status. There is great degree of variations in nature and severity of pain reported by patient in otherwise similar underlying pathology. Clinical reasoning and decision making is done depending on the nature or characteristics of pain reported by the patient [2]. There is often a variable and inconsistent relationship between pathology and pain. For example, pain is present in the absence of or disproportionate to the underlying pathology and persistence of pain after the resolution of injury or pathology. Also severity of pain in some patients differs greatly if we compare it with others having similar injuries and pathologies where there is no evidence of injury or pathology [3,4]Neurophysiologic mechanisms like 'Gait control theory of pain' (described by Melzack and Wall), explains the modulation of pain transmission which occurs on the dorsal horn of the spinal cord [5, 6]. Contemporary approaches like 'bio psychological model' [7, 8] and 'mechanism- based approaches' [9, 10], along with the gate control theory of pain attempt to explain the relationship between pain perception and the underlying pathology. Mechanisms-based approach classifies pain mechanisms as : Peripheral nociceptive (mechanical or inflammatory), Neurogenic sensitisation (peripheral and central), Autonomic and Behavioural [10, 11] Clinical interventions which are known or hypothesized to target the dominant underlying neurophysiologic mechanisms responsible for its generation and maintenance, could improve treatment of pain and optimize patient's outcomes [12]. Acute pain originates from nociceptors in somatic or visceral tissue. If this pain persists beyond the expected tissue healing time following an injury or surgery is considered chronic pain. However the exact time frame constituting an expected healing period is variable and it is difficult to mention. It has been suggested that if pain persists beyond 3 to 6 months time window, it is considered as a chronic pain [13]The aetiology, pain intensity and impact of pain are also considered as additional factors affecting the chronicity. An alternative way to characterize chronic pain is, whether it has emerged as a result of peripheral and central reorganization.

II. Central Sensitization (CS)

The nervous system shows the simplest form of plasticity. To a repeated painful or noxious stimulation it can exhibit habituation (decreased response) or sensitization (increased response). Nervous system sensitization can be peripheral or central. Central sensitization is due to increased excitability of pathways localised in the spinal cord and the brain. Central sensitisations cause multiple effects. It causes malfunctioning of pain inhibitory mechanisms and altered sensory processing [14, 15]. Chemical, electrophysiological and pharmacological system's function may get altered due to neuroplasticity and subsequent CNS sensitization. These changes can manifest as hyperalgesia, allodynia or referred pain. Exacerbation and recurrence of pain occur due to cortical mapping and pre-sensitization as it possesses a pain 'memory' [14, 16-20]. Observational brain studies, cerebral metabolism studies and psychophysical testing with various stimuli show that CS is present in patients with chronic pain [21-29]. Patients with low back pain [30-32], Persisting neck pain [33-36],

osteoarthritis [37, 38], rheumatoid arthritis [39], fibromyalgia [40, 41], tennis elbow [42, 43], subacromial impingement syndrome [44], and patella tendinopathy [45] and pelvic pain [46] show features of central sensitization.

In some patients, peripheral inputs maintain pain while in others it is maintained by central changes; however majority of patients show combination or overlap between both. Furthermore, changes in the peripheral nervous system can create alterations in the CNS and vice versa. For example, non- inflammatory muscle pain does not show local inflammation, but it has a strong central pain component which is independent of peripheral afferent input. On the other hand, in patients with rheumatoid arthritis inflammatory joint pain is significant. It has a strong peripheral component and it involves sensitization of nociceptors by inflammatory cytokines [47, 48]. Therefore, activation of both peripheral and central pain pathways is seen in chronic musculoskeletal pain. Therefore it is very important to assess the each component while formulating the treatment plan for the patient.

III. Assessing Central Sensitization (CS) In Clinical Practice

CS modulates the development of pain. It can cause transition from acute to chronic pain [49, 50]. As discussed, patients with chronic pain are more likely to present with CS but it may be present in acute or sub-acute stages as well. For example, abnormal sensory processing may appear rapidly after the initial whiplash trauma (less than 7 days) in patients with whiplash associated disorders and chronicity may develop in later stages [51, 52]. Therefore, it is important for physiotherapists to find out CS in patients in the early stage/ sub-acute stage as well.

To find out the component of CS Jo Nijs et al [53] have highlighted the importance of the excluding neuropathic pain and the differentiating nociceptive from CS pain. Patients with neuropathic pain gives history of a disease or lesion of the nervous system and diagnostic investigations show abnormality of the nervous system or post-surgical or post- traumatic damage to the nervous system. Pain and location of the sensory dysfunction is neuro-anatomically logical and described as shooting, burning or prickling whereas non-neuropathic CS shows no history of a lesion or any disease of the central nervous system. Diagnostic investigations show no abnormality of the nervous system. Pain is vague and dull and location of the sensory dysfunction is not neuro-anatomically logical. There are areas with increased sensitivity which are unrelated to the primary source of pain in non-neuropathic CS [54]. Nociceptive pain shows evidence of injury or pathology which is proportionate to the severity of pain and perceived disability whereas CS is characterized by pain disproportionate to the nature and extent of injury. Jo Nijs et al [54] laid down following criteria to favour CS as
Criterion 1: Pain experience disproportionate to the nature and extent of injury or pathology
Criterion 2: Diffuse pain distribution, allodynia, and hyperalgesia
Criterion 3: Hypersensitivity of senses unrelated to the musculoskeletal system.

If criterion 1 and 2 are both met, then the classification of CS can be established. If only the first criterion (disproportionate pain) is met and not the second criterion, further screening of criterion 3 is required. There are additional signs which can be present in patients with CS like numbness, muscle weakness, cognitive deficits, sleeping difficulties, dyskinaesthesia, inconsistent clinical examination findings, impaired tactile localization, phantom swelling sensation, swelling enhancement and swelling diminishment, phantom stiffness and altered perception of affected body part. There is an association between CS and maladaptive psychosocial factors such as negative emotions, poor self-efficacy, maladaptive beliefs and pain behaviours [54, 55]. Patients may show unpredictable or inconsistent or absence of response to nociception-targeted treatments. They may also even show exacerbation of their signs and symptoms to treatments [54, 55].

IV. Targeting CS In Clinical Practices

Patient education:

Elevated fear-avoidance beliefs are a maladaptive emotional response towards an excessive fear of pain that can eventually lead to avoidance behaviour. Avoidance refers to behaviour which is aimed at postponing or preventing an unpleasant situation from occurring. Pain catastrophizing is the tendency to fear the worst. A vicious circle may be initiated when the pain is catastrophically misinterpreted [56-59]. These dysfunctional interpretations give rise to pain-related fear, and associated safety seeking behaviours such as avoidance/escape and hypervigilance, that can be adaptive in the acute pain stage and worsen the problem in the case of long-lasting pain [60]. Patient education helps to build confidence and positive beliefs which tend to improve their physical performances [61]. Moseley proposed a pain neuromatrix approach [61] to manage patients with chronic pain. A series of high-quality randomized controlled trials [62-65] found that Pain Physiology Education (PPE) decreased pain intensity in chronic low back pain patients.

Manual therapy:

Tissue injury healing and local pain recovery should occur within a period of approximately 3 months. So it is important to use appropriate manual therapy techniques in acute/ sub-acute conditions which will help to

resolve localised pain. CS can cause decreased sensory threshold therefore exercise program and hands- on technique should be decided accordingly. Any treatment which aggravates painful inputs can trigger the process of CS. Soft tissue mobilisation is helpful in chronic widespread pain or fibromyalgia. It helps to release restrictions and restore blood flow where trigger points are present. The area of the trigger points have lower pH value and increased levels of substance P, tumour necrosis factor and interleukin etc. which are known to increase sensitivity. So they may respond to even weak stimulus [66]. Therefore, soft tissue mobilisation can be started at superficial level with strokes along the length of the muscle fibres and then progressing towards deeper strokes which go perpendicular to the soft tissue fibres [67].

Breathing:

Deep breathing retraining is believed to down-regulate the sensitive nervous and sympathetic nervous system [68].

Exercise:

Vigorous exercises can activate joint and muscle nociceptors, which can send continuous painful stimulus and cause sensitization [54]. Aerobic exercises help to lower a person's stress response. It also assists in mood and anxiety relief [69, 70]. Staud R et al also demonstrated that isometric and aerobic exercises activate endogenous opoid and adrenergic pain-inhibitory mechanisms in healthy subjects, while it increases experimental pain ratings in patients having fibromyalgia [71]. Therefore, exercise program should be planned very cautiously so that CS should not amplify.

Motor control re-training:

Motor control retraining in symptomatic joints can also prevent chronicity. For example, presence of impaired motor control in the end- range movement can repetitively cause micro trauma and serve as an on-going source of pain. This may aggravate sensitivity and may trigger CS [54, 73, 74].

Relaxation and improving stress tolerance:

Chronic pain and psychosocial changes can cause stress. Relaxation helps to manage stress and anxiety through the central dis-inhibitory mechanism. Also helps to decrease their deleterious effects on the sympathetic nervous system [75, 76]. Reduction of stress levels can significantly improve the patient's pain threshold, their maladaptive behavioural responses and autonomic balance [77, 78].

Virtual reality:

Evidence of its clinical application is limited. Helpful in patients with movement associated pain. Its effect is thought to achieve from distraction in the hyper-vigilant patient [79].

Medications:

Centrally-acting drugs like serotonin and norepinephrine reuptake inhibitor drugs, the serotonin precursor tryptophan, opioids and NMDA-receptor antagonists are indicated for the treatment of CS.

V. Conclusion

Physiotherapists should emphasis on mechanism based treatment approach to understand & manage patients effectively. The awareness of CS plays an important role in the management of chronic pain. Therefore, the process of the CS should also be considered in the treatment or rehabilitation in patients with chronic musculoskeletal pain.

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