Recognition and Treatment of Central Sensitization in Chronic Pain Patients: Not Limited to Specialized Care

Modern pain neuroscience has advanced our understanding about pain, including the role of central sensitization (CS) or central hyperexcitability in the presence and amplification of pain experiences. Central sensitization is defined as “an amplification of neural signaling within the central nervous system that elicits pain hypersensitivity”\(^2\) and “increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input.”\(^7\) Though these definitions originated from laboratory research, nowadays the pain field has more or less accepted the need for, and comprehends the importance of, translating the concept of CS to the clinic.

The implementation of modern pain neuroscience in practice is a hot topic, and musculoskeletal physical therapists around the world are at the front line of this process. However, many clinicians struggle to implement modern pain neuroscience during the assessment, clinical reasoning, and treatment of patients with chronic pain. Some even argue that CS is seldom seen among patients in primary care and the implementation is therefore primarily focused on specialized pain management programs. Here, we make a plea for a much wider implementation of modern pain neuroscience, with special emphasis on CS, into general musculoskeletal practice. We have done this by explaining the main psychophysiological mechanisms underlying CS, summarizing the main research findings regarding the role of CS in patients within an orthopaedic or sports setting, and discussing the challenging issue of clinical recognition of CS by physical therapists. Finally, the main treatment implications for our profession are highlighted.

Understanding the Psychophysiology of CS

In many patients with chronic pain, a clear origin for nociceptive input is lacking or is not severe enough to explain the severe pain and other symptoms experienced by the patient. In such patients, CS is often present and can explain the clinical picture. Central sensitization encompasses various related dysfunctions within the central nervous system, all contributing to altered (often increased) responsiveness to a variety of stimuli, such as mechanical pressure, chemical substances, light, sound, cold, heat, stress, and electricity.\(^2\) Such central nervous system dysfunctions include altered sensory processing in the brain,\(^3\) with in-
creased brain activity in areas known to be involved in acute pain sensations (insula, anterior cingulate cortex, and prefrontal cortex), as well as in regions not involved in acute pain sensations (various brain stem nuclei, dorsolateral frontal cortex, and parietal-associated cortex); poor functioning of descending antinociceptive mechanisms ("the brake"); and increased activity of brain-orchestrated nociceptive facilitatory pathways ("the accelerator"). The accelerator is further activated by cognitive-emotional factors, such as pain catastrophizing, stress, hypervigilance, lack of acceptance, depressive thoughts, and maladaptive illness perceptions (eg, perceived injustice).

Taken together, in patients with predominant CS and chronic pain, the brake is no longer functioning properly and/or the accelerator is way too active. This results in an exaggerated central nervous system response (severe pain often accompanied by various other symptoms, such as sleep disturbances and stress intolerance) to little (nociceptive) or normal (nonnociceptive) somatosensory input.

**In Which Patients Can We Expect to Find CS?**

In the field of orthopaedic and sports physical therapy, potentially every pain patient may develop CS, but only a minority will. Patients who do not recover spontaneously from a whiplash injury most often present a clinical picture dominated by CS, and fibromyalgia probably represents the extreme of the continuum. In other chronic pain conditions, such as low back pain, tendon problems, shoulder pain, osteoarthritis, rheumatoid arthritis, pain following cancer treatment, tennis elbow, and headache, predominant CS is present in a minority. Examples like persistent rotator cuff (shoulder), lateral elbow, patellar, and Achilles tendinopathies, where CS is often present, indicate its presence also in the field of sports. Here, clinicians need to examine each patient individually and should recognize predominant CS when present.

Some may wonder whether CS is of clinical importance or whether it is merely an epiphenomenon. Three lines of evidence support its clinical importance: (1) compared to those without signs of CS, patients with chronic pain with predominant CS have much higher pain severity and lower quality of life; (2) CS predicts poor outcome in various patients with chronic musculoskeletal pain, including tennis elbow, chronic pain following whiplash injury, and osteoarthritis; and (3) CS mediates treatment outcome in patients with low back pain, whiplash, and osteoarthritis. Taken together, accumulating evidence supports the clinical importance of CS in people with chronic musculoskeletal pain, especially in the field of orthopaedics and sports. People with predominant CS pain have a poor prognosis and do not respond to local treatment. Therefore, it is of prime importance that we identify those patients during the initial screening. This will be explained in the next section.

**Recognition of CS in Clinical Practice**

Broadly, 4 pain classifications are widely considered: nociceptive (inflammatory) pain, neuropathic pain, CS pain, and mixed pain. For clinical purposes, the term nociceptive pain can be used when pain is proportional to nociceptive input, whereas neuropathic pain is defined as pain caused by a primary lesion or disease of the somatosensory nervous system. Recently, a clinical method for classifying any pain as predominant CS, neuropathic, or nociceptive pain was developed, based on a large body of research evidence and international expert opinion. The first step includes screening for neuropathic pain. Guidelines for the classification of neuropathic...
pain are available. The criteria specify that a lesion or disease of the nervous system (either central or peripheral) is identifiable and able to explain the clinical picture that the patient is presenting, that is, that the pain is limited to a “neuroanatomically plausible” distribution and is supported by both the clinical examination findings and findings from imaging and laboratory testing. For instance, when objective evidence supports a lesion of the nervous system (eg, amputation or damaged spinal cord) but cannot fully (neuroanatomically) explain the widespread symptoms the patient is experiencing, then the patient might have a mixed type of pain (perhaps neuropathic plus CS pain).

In cases without neuropathic pain or with a mixed type of pain, screening for nociceptive and CS pain is the next step. To differentiate predominant nociceptive and CS pain, clinicians are advised to use the algorithm shown in the figure, guiding them through the screening of 3 major classification criteria, each of which is explained below.

**Criterion 1: Pain Experience Disproportionate to the Nature and Extent of Injury or Pathology**

Per definition, CS pain is disproportionate to the nature and extent of injury or pathology, making it a go or no-go criterion for CS pain. For screening this first criterion, it is necessary to assess the individual’s amount of injury, pathology, and objective dysfunction capable of generating nociceptive input. This includes identifying such nociceptive sources (eg, X-rays, computed tomography scan, and nuclear magnetic resonance imaging) and interpretation of the clinical examination. The next step involves considering whether the amount of injury, pathology, and objective dysfunction capable of generating nociceptive input is sufficient to explain the patient’s subjective pain experience. In many patients, the clinical examination and/or imaging reveals some type of potential nociceptive source, which makes thorough clinical reasoning necessary for weighing the nociceptive input against the pain experienced. This includes taking into account all personal and environmental factors.

**Criterion 2: Neuroanatomically Illogical Pain Pattern**

A neuroanatomically illogical pain pattern is present when the patient presents with a pain distribution that is not neuroanatomically plausible for the presumed source(s) of nociception. Not neuroanatomically plausible relates to allodynia and/or hyperalgesia outside the segmental area of primary nociception. For screening this criterion, a thorough assessment and interpretation of the patient’s self-reported pain distribution, in light of the identified possible sources of nociception, are required. Pain drawings can be used to standardize and optimize the assessment of the individual’s pain distribution in a reliable way. The body of research supporting spreading pain outside the area of presumed nociception as a cardinal feature of CS pain continues to grow.

**Criterion 3: Hypersensitivity of Senses Unrelated to the Musculoskeletal System**

Given the overall hyperresponsiveness of central nervous system neurons, CS may explain the altered sensitivity to many environmental (bright light, cold/heat, sound/noise, weather, stress) or even chemical (odors, pesticides, medication) stimuli. For assessing sensory hypersensitivity, the Central Sensitization Inventory can be used. Several studies support the clinimetric properties of the Central Sensitization Inventory in different countries. The cutoff of 40/100 allows correct identification of over 82% of patients with CS pain, but the chances of false positives are relatively high, which supports our approach of combining this measure with a more comprehensive examination for identification of predominant CS pain.

Since the initial publication of the classification criteria for musculoskeletal pain in general, they have been adapted to better fit the specific needs for the clinical classification of pain types in people with low back pain and pain following cancer treatment. A group of osteoarthritis experts from 5 countries is currently adapting them for the emerging field of osteoarthritis pain. Still, despite their initial success and fundamental science, studies exploring the clinical validity (ie, test-retest reliability, interobserver reliability, concurrent validity, content validity, etc) are needed.

**Treatment Implication of CS in Orthopaedic and Sports Physical Therapy**

Knowing that CS predicts poor (treatment) outcome in various populations of chronic musculoskeletal pain, it seems rational to account for CS during treatment. How exactly should orthopaedic and sports physical therapists account for CS in clinical practice? First, treatment strategies that aim at targeting local structures (ie, within the painful anatomical region) are typically of little value in those with predominant CS pain. Hence, a more “central” approach targeting brain and top-down mechanisms seems warranted for treating CS in patients with musculoskeletal pain. This applies to conservative as well as to pharmacological interventions. Second, patients with severe and spreading pain, as typically seen in CS, often ruminate about their pain (and why they do not respond to local treatments). Therefore, the first step of treating CS often comprises explaining pain (ie, pain neuroscience education). This allows patients to understand their condition and to improve their pain beliefs and coping strategies. Third, subsequent to the initial educational treatment phase, active interventions such as stress management, sleep management, graded activity/graded exercise therapy, and graded exposure may benefit patients with predominant CS pain. For therapists who consider using hands-on manual therapy, possibly because of its short-term effects on top-down nociceptive inhibition, aligning the communication surrounding the application of manual therapy seems warranted. Finally, given the cardinal role of cognitive-emotional factors (eg, pain catastrophizing, anxiety, maladap-
tive pain beliefs, maladaptive pain coping strategies, anger, perceived injustice) in sustaining (and possibly also initiating) CS in patients with musculoskeletal pain, the comprehensive treatment plan should target those factors (in some cases, even more than it should target the mechanism of CS). For more detailed practical guidelines on how to treat CS in patients with chronic musculoskeletal pain, readers are referred to other publications.  

CONCLUSION

In conclusion, modern pain neuroscience has substantially improved our understanding of the (development of) chronic musculoskeletal pain. The time has come for orthopaedic and sports physical therapists to implement modern pain neuroscience in specialized, but definitely also in primary, care settings, including the role of CS in amplifying and explaining the presence of the pain experience. Evidence supporting the clinical importance of CS in patients with musculoskeletal pain is accumulating. Central sensitization dominates the clinical picture in a subgroup of the musculoskeletal pain population, ranging from tennis elbow over shoulder pain to osteoarthritis and whiplash. Applying modern pain neuroscience to clinical practice implies (1) recognizing those patients having predominant CS pain, and (2) accounting for CS when designing the treatment plan in those with predominant CS pain. Future work in this area should (1) examine the validity of the proposed clinical classification algorithm for identifying CS pain in patients with orthopaedic and sports injuries, and (2) explore evidence-based treatment options for patients having predominant CS pain. 

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