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MASTERCLASS

# Modern pain neuroscience in clinical practice: applied to post-cancer, paediatric and sports-related pain

Anneleen Malfliet[a,b,c,d,*], Laurence Leysen[a,b], Roselien Pas[a,b,e], Kevin Kuppens[b,e], Jo Nijs[a,b,d], Paul Van Wilgen[a,b,f], Eva Huysmans[a,b], Lisa Goudman[a,b,g], Kelly Ickmans[a,b,d]

[a] *Department of Physiotherapy, Human Physiology and Anatomy (KIMA), Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Belgium*
[b] *Pain in Motion International Research Group,[◊] Belgium*
[c] *Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, Ghent University, Belgium*
[d] *Department of Physical Medicine and Physiotherapy, University Hospital Brussels, Belgium*
[e] *Department of Rehabilitation Sciences and Physiotherapy (REVAKI), Faculty of Medicine and Health Sciences, University of Antwerp, Belgium*
[f] *Transcare, Transdisciplinary Pain-management Centre,[◊◊] The Netherlands*
[g] *Department of Neurosurgery, University Hospital Brussels, Brussels, Belgium*

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**Abstract**
*Background:* In the last decade, evidence regarding chronic pain has developed exponentially. Numerous studies show that many chronic pain populations show specific neuroplastic changes in the peripheral and central nervous system. These changes are reflected in clinical manifestations, like a generalized hypersensitivity of the somatosensory system. Besides a hypersensitivity of bottom-up nociceptive transmission, there is also evidence for top-down facilitation of pain due to malfunctioning of the endogenous descending nociceptive modulatory systems. These and other aspects of modern pain neuroscience are starting to be applied within daily clinical practice. However, currently the application of this knowledge is mostly limited to the general adult population with musculoskeletal problems, while evidence is getting stronger that also in other chronic pain populations these neuroplastic processes may contribute to the occurrence and persistence of the pain problem. Therefore, this masterclass article aims at giving an overview of the current modern pain neuroscience knowledge and its potential application in post-cancer, paediatric and sports-related pain problems.


* Corresponding author at: Vrije Universiteit Brussel, Medical Campus Jette, Building F-Kine, Laarbeeklaan 103, BE-1090 Brussels, Belgium.
*E-mail:* Anneleen.Malfliet@vub.ac.be (A. Malfliet).
◊ www.paininmotion.be.
◊◊ www.transcare.nl.

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## Introduction

Modern pain neuroscience has raised the awareness that pain and tissue damage are not synonymous terms. Pain is often disproportionate to tissue damage and can even be reported without it. On the other hand, obvious tissue damage (and thus nociception) does not guarantee the actual feeling of pain either. Many chronic pain patients present a generalized hypersensitivity of the somatosensory system, often referred to as central sensitization.[1–4] Central sensitization is not only present in typical chronic widespread pain conditions such as chronic fatigue syndrome[5] and fibromyalgia,[1,6] but is also known to be the underlying mechanism in at least a subgroup of patients with persistent low back pain,[7,8] migraine,[9] pelvic pain,[10,11] tennis elbow,[12] subacromial impingement syndrome,[13] post-cancer pain[14] and rheumatoid arthritis.[15]

Central sensitization can include neuroplastic changes in both the peripheral and central nervous system. Besides increased neuronal responsiveness in the periphery and spinal cord (e.g., enhanced bottom-up signalling),[16,17] an important role within the pathophysiology of central sensitization is reserved for malfunctioning of the endogenous descending nociceptive modulatory systems.[18,19] The basis of this nociceptive modulatory system is situated in the brain, where it seems to present itself in a 'neurologic pain signature'. While several pain areas are involved in pain processing and modulation, certain cognitive styles and personality traits influence this system through complex collaboration between the prefrontal cortex, limbic system and periaqueductal grey among other brain areas.[20] In these and other nociceptive-processing brain areas, abnormalities in structure and function are described within several chronic pain populations.[21–24] Nevertheless, evidence in several chronic pain populations indicates that these observed abnormalities are a reversible consequence of chronic pain rather than actual damage. In fact, recent studies investigating the effect of surgical interventions in chronic pain patients demonstrate for example that grey matter abnormalities subside with the cessation of pain.[25,26] Moreover, conservative treatments such as physical therapy interventions are able to alter abnormalities of the central nervous system.[27–30]

The current progress in pain neuroscience knowledge increases the need for its implementation in daily clinical practice. Not only is it relevant to understand the influencing mechanisms in chronic pain, the presence of central sensitization has also been identified as a predictor for poor therapy outcome.[31–33] Therefore, targeting the processes underlying central sensitization becomes an important consideration in clinical practice. Several therapy modalities are suggested for chronic pain management, but the absolute first step should always comprise pain neuroscience education.[34,35]

Pain neuroscience education includes explaining to patients that pain is an output product of the brain resulting from input from multiple central and peripheral nervous system processes and leading to the perception of threat rather than pain being a reflection of current tissue damage.[36] Pain neuroscience education intends to transfer that knowledge to patients, allowing them to understand their pain and hence to effectively cope with their pain.[36] Educating the chronic pain patient on the neuroscience behind their symptoms has been shown to be both comprehensible and effective.[37,38] Although pain neuroscience education is necessary to overcome initial treatment barriers (perceptual context of a patient related to the identity, cause and consequences of the illness) and to increase therapy compliance, effect sizes remain rather small.[38–42] Therefore it should not be used as sole treatment, but rather as a component in an active therapy programme with special emphasis to maladaptive pain perceptions and cognitions.[34,43]

In a manual (or musculoskeletal) therapy setting, this active component can easily be implemented by providing the usual exercise and treatment modalities adjusted with modern pain neuroscience. This includes a time-contingent approach where cognitions and perceptions related to the specific exercise are constantly assessed and addressed when necessary. Because of the rather accessible implementation in manual (or musculoskeletal) therapy, the application of modern pain neuroscience is to date mostly concentrated in this area of physical therapy. However, central sensitization is not limited to merely musculoskeletal pain in a general adult population, but has also been described in post-cancer,[14] pediatric[44–52] and sports-related pain problems.[53] Therefore, this masterclass article aims to provide a critical overview on the application of modern pain neuroscience in post-cancer, paediatric and sports-related pain.

## Modern pain neuroscience applied to post-cancer pain

In addition to fatigue, pain is the most persistent symptom in cancer survivors.[54] Classification of cancer pain used to be a controversial issue.[55] In recent years, a paradigm shift towards a mechanisms-based approach has taken place in the field of cancer pain,[56] analogue to evolutions in other chronic pain conditions.[57,58] For effective pain management, correct identification of the dominant type of pain may be beneficial. Patient-centred physical therapy for cancer pain, founded on a mechanisms-based classification of pain, has previously been shown to yield positive findings in a prospective case series.[59] Such mechanism-based pain classification includes the differentiation between nociceptive, neuropathic and central sensitization pain.[56,60] Recently, a clinical method for classifying any pain as either predominant central sensitization pain, neuropathic or nociceptive pain[2] was adopted to the cancer survivor population,[61] allowing clinicians to differentiate between these three pain types. Since neuropathic and mixed cancer pain (i.e., a mixture of nociceptive, neuropathic and/or central sensitization pain) are considered to be more difficult to treat than pure nociceptive pain,[62,63] this is important for clinical practice. Furthermore, the classification of the correct pain mechanism is relevant regarding the choice of the cancer pain treatment.[63]

In addition to the classification of the predominant pain mechanism, modern pain neuroscience provides ample options for innovation within the field of physical therapy for people with pain following cancer treatment, including innovative educational, stress management and exercise interventions.



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