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From non-specific low back pain to chronic primary musculoskeletal low back pain: the evolving concept

*[1,3]Svetlana Plesca, [3]Oxana Grosu, [2,3]Marina Sangheli

[1,3]Department of Medical Rehabilitation, Physical Medicine and Manual Therapy, [2]Department of Neurology No 1, *Nicolae Testemitanu* State University of Medicine and Pharmacy
[3] *Diomid Gherman* Institute of Neurology and Neurosurgery, Chisinau, the Republic of Moldova

Authors' ORCID iDs, academic degrees and contribution are available at the end of the article

*Corresponding author – Svetlana Plesca, e-mail: svetlana.plesca@usmf.md
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Abstract

Background: Low back pain (LBP) for many years is considered one of the most common conditions causing work absenteeism and long-term disability, with important implications for public health systems and economies. Pain generators of LBP are various, being distinguished specific and non-specific causative mechanisms. The term "non-specific" LBP remains ambiguous as potential sources of pain are supposed to be muscles or joints, but supplementary investigations do not correlate enough to explain the pain intensity and disability. The nociceptive and/or neuropathic mechanisms characteristic for acute pain tend to be influenced by central sensitization while pain chronification occurs, leading to new descriptor as nociplastic pain. Chronic low back pain, considered mostly non-specific, was mechanistically referred to primary musculoskeletal low back pain, the concept introduced in the new ICD-11 classification. The process of acceptance by the scientific medical community raised debates and discussions. The aim of the study was to analyze the evolving concept of non-specific low back pain to chronic primary musculoskeletal low back pain. A narrative literature review was carried out.
Conclusions: The term non-specific low back pain is used when the pain generators have not been accurately determined or cannot fully explain the existing symptomatology. Chronic primary musculoskeletal low back pain is better explained by central sensitization mechanisms and altered nociception, named nociplastic pain. Because of raised ambiguities regarding this concept further studies are expected to shed light on the problem.
Key words: non-specific low back pain, chronic primary musculoskeletal low back pain, central sensitization.

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Introduction

Low back pain (LBP) for many years is considered one of the most common conditions causing work absenteeism and long-term disability, with important implications for public health systems and economies [1]. In accordance with the Global Burden of Disease study LBP was the leading cause of years lived with disability with estimated prevalence of 7.5% of the global population, or around 577 million people [2].

Low back pain is defined as *"pain in the area on the posterior aspect of the body from the lower margin of the twelfth ribs to the lower gluteal folds with or without pain referred into one or both lower limbs that lasts for at least one day"* [3]. Many potential anatomic sources, such as nerve roots, muscle, fascial structures, bones, joints, intervertebral discs, and organs within the abdominal cavity are known as pain generators for LBP [4]. Because of its complexity, diagnostic evaluation of the patient with LBP is a real challenge. Furthermore, identifying the anatomical source of pain is of major importance in determining management strategies. This is especially true when there are specific pathophysiological mechanisms of non-spinal (hip conditions, diseases of the pelvic organs, aortic aneurysm) or spinal origin (herniated disk, spinal stenosis, fracture, tumor, infection, spondylarthritis) [5].

In cases of unidentified causes of LBP, it is referred to as non-specific one. According to International Association for the Study of Pain (IASP) this term is known as "Lumbar Spinal Pain of Unknown or Uncertain Origin". Over the years, authors provide references based on various studies about the lack of etiology of these conditions as being about 85-90%, compared to specific etiology [6].

Certain ambiguities in understanding the classification of LBP are created as well by the fact that some scientific sources classify this condition as mechanical and non-mechanical, or musculoskeletal and neurological [7, 8]. It is observed that most of the studies identified similarity between non-specific low back pain and mechanical or musculoskeletal LBP, taking into account the main underlying mechanisms. The source of musculoskeletal (non-neurologic) back pain is often non-specific and difficult to identify in most patients. It is considered that pain arises from degenerative spine changes and injury to

local spinal structures, which include the vertebral column, ligaments, and surrounding muscles and soft tissues. In such cases the main pain generators are nociceptors localized in these structures.

At the same time, LBP could cover other spectrum of pain, such as neuropathic pain irradiating down the leg in case of radiculopathy and, in some cases, nociplastic pain, which is caused by amplification of pain in the CNS, especially when chronicity occurs. Frequently, these pain subtypes overlap (e.g., a patient with a herniated disc who has back pain can have radicular pain and diffuse symptoms outside pathoanatomical referral patterns) [9].

In the majority of cases acute low back pain is self-limiting, and prognosis is relatively favorable [10]. Chronic pain goes beyond the period of repair of tissue damage that occurred during the acute stage. According to published data, 2% to 48% (median, 26%) of patients with acute LBP in primary care settings become chronic [11]. Chronic pain is often non-specific, implying that there is no pathology or tissue damage or that the limited amount of pathology or tissue damage is not severe enough to explain the pain experience [12].

LBP is termed as chronic when persisting >3 months, being no longer considered as a symptom, but as a disease caused by numerous onset factors. A vast majority of patients (45–75%) report feeling pain 12 months after the onset of LBP, transforming the LBP into the most common musculoskeletal diseases among people with chronic pain [13]. According to the World Health Organization (WHO), 20–33% of the world's population have some form of chronic musculoskeletal pain [14]. The transition of acute pain to chronic is a dynamic process based on mechanisms of amplification of noxious and non-noxious stimuli, described as central sensitization (CS) [15, 16]. IASP definition of CS is "increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input" [17]. The concept of CS can explain the discrepancy between the experienced pain severity, disability or other symptoms and the minor degree of tissue damage or suffering from pain in the absence of a clear origin of nociceptive input [12, 18].

The historical evolution of the various theories explaining the pain phenomenon, e.g., "the gate control theory", the concept of neuromatrix described by Melzac and others leads to the conclusion that chronic low back pain is not only an experience induced by the direct nociceptors painful stimulus but represents a multidimensional process with the involvement of biological, psychological, and social factors. From the biopsychosocial model of pain perspective, such factors as biological (genetic factors, comorbidities, etc.), psychological (anxiety, depression, cognitive beliefs, coping skills) and social (financial barriers, job satisfaction) are associated with the development of chronic pain, but at the same time can be the result of chronic pain [19, 20].

The recently published International Statistical Classification of Diseases and Related Health Problems (ICD) codes, ICD-11 identifies chronic pain as a stem code, with chronic primary pain a subcategory that can occur in one or more anatomical regions independently of identifiable biological or psychological contributors [21-23]. The low back pain has been devoted to primary chronic pain section as both diagnostic and treatment concepst have changed.

The aim of the study was to analyze the evolving concept of non-specific low back pain to chronic primary musculoskeletal low back pain.

The literature search was performed in PubMed, Web of Science and Scholar databases. The search terms were: `*low back pain*`, `*chronic low back pain*`, `*classification chronic low back pain*`, `*definition chronic low back pain*`. Articles were selected for the 20-year period and in English. The search for `*low back pain*` term returned 35.496 results, RCT`s – 3.112. The search for `*chronic low back pain*` term returned 12.545 results and RCT`s – 1.673. The search for `*classification chronic low back pain*` term returned 582 results, and `*definition chronic low back pain* ` term returned 328 results. All the titles and abstracts were screened and suitable articles were extracted and analyzed. The principal themes are presented in the article.

Results and discussion

The Pain Task Force of the IASP defines chronic primary pain as pain in one or more anatomical regions that persists or recurs for longer than 3 months, and that is characterized by significant emotional distress (anxiety, anger/frustration or depressed mood) or functional disability (interference in daily life activities and reduced participation in social roles) [17, 22].

Diagnostic criteria for chronic primary pain [24].

Conditions A to C are fulfilled:

A. Chronic pain (persistent or recurrent for longer than 3 months) is present
B. The pain is associated with at least one of the following:
B.1 Emotional distress due to pain is present.
B.2 The pain interferes with daily life activities and social participation.
C. The pain is not better accounted for by another chronic pain condition.

Chronic primary musculoskeletal (MSK) pain is a stem category of chronic primary pain and is defined as chronic pain in the muscles, bones, joints, or tendons that is characterized by significant emotional distress (anxiety, anger/frustration or depressed mood) or functional disability (interference in daily life activities and reduced participation in social roles). Chronic primary MSK pain is divided into chronic primary low back pain, chronic primary cervical pain, chronic primary thoracic pain, chronic primary limb pain [22, 24].

The diagnosis of chronic primary MSK pain is appropriate independently of identified biological or psychological contributors unless another diagnosis would better

account for the presenting symptoms. The new classification of chronic primary MSK pain provides an opportunity to categorize, diagnose, and treat musculoskeletal pain conditions previously referred to as "non-specific" [22, 25]. Primary MSK pain is neither nociceptive nor neuropathic, as involvement of nociceptors or somatosensory system is not detected, but in which clinical and psychophysical findings suggest altered nociceptive function. Such mechanism was referred to a new concept of pain pathophysiology named nociplastic pain [22].

Nociplastic pain is defined 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 [26]. Kosek E. et al. [27] proposed clinical criteria to identify nociplastic pain affecting the musculoskeletal system (chronic primary MSK pain) (tab. 1):

Low back pain is a complex problem that includes conditions with different etiologies, evolution, and evolving mechanisms. Taken together, these mechanisms are a substantial burden on the patient, society and health care systems. The acute and subacute evolution of pain, with the duration of the pain phenomenon up to 6-12 weeks, is often related to "non-specific" or mechanical causes, when the involvement of the muscular and osteoligamentary systems (myofascial syndrome, zygoapophisal joints and intervertebral disc degeneration) lead to nociceptive pain. At the same time, mechanical low back pain could be specific in origin, as it is in disc herniation or lumbar spine stenosis with neuropathic pain component. The involvement of different structures responsible for onset of lumbar pain, but also different types of its evolution, outline various pain characteristics, such as nociceptive pain, neuropathic pain or nociplastic pain, and in some cases mixed forms of manifestation.

Table 1. Clinical criteria and grading for nociplastic pain affecting the musculoskeletal system [27]

1. The pain is:
1a. Chronic (>3 mo);
1b. Regional (rather than discrete) in distribution*;
1c. There is no evidence that nociceptive pain (a) is present or (b) if present, is entirely responsible for the pain;
1d. There is no evidence that neuropathic pain (a) is present or (b) if present, is entirely responsible for the pain.†
2. There is a history of pain hypersensitivity in the region of pain. Any one of the following:
Sensitivity to touch
Sensitivity to pressure
Sensitivity to movement
Sensitivity to heat or cold
3. Presence of comorbidities. Any one of the following:
Increased sensitivity to sound and/or light and/or odors
Sleep disturbance with frequent nocturnal awakenings
Fatigue
Cognitive problems, such as difficulty to focus attention, memory disturbances, etc.
4. Evoked pain hypersensitivity phenomena can be elicited clinically in the region of pain. Any one of the following:
Static mechanical allodynia
Dynamic mechanical allodynia
Heat or cold allodynia
Painful after-sensations reported following the assessment of any of the above alternatives.
Possible nociplastic pain: 1 and 4.
Probable nociplastic pain: all the above (1, 2, 3, and 4)‡

* – Musculoskeletal pain is deep, rather than cutaneous and regional, multifocal, or widespread in distribution (rather than discrete). In case of multifocal pain states that can be caused by different chronic pain conditions (e.g., shoulder myalgia and knee osteoarthritis), each chronic pain condition or pain region must be assessed separately.

† – The presence of a source of nociceptive pain, such as osteoarthritis, or of neuropathic pain, such as a peripheral nerve lesion, does not exclude the concurrence of nociplastic pain, but the region of pain must be more widespread than that which can be explained by the identifiable pathology.

‡ – The purpose of the grading system is to indicate the level of certainty that a patient has nociplastic pain and, as mentioned above, was inspired by the current grading system for neuropathic pain. However, because of the lack of clinically useful, reliable diagnostic tests to confirm the presence of altered nociception, currently nociplastic pain is graded as possible or probable but not definite. If future diagnostic tests are developed and validated, the introduction of the term "definite nociplastic pain" should be considered.

The scientific debates on back pain are mostly related to terminology. This is observed from the stage of understanding low back pain as "non-specific" with nociceptive mechanism, in which the involvement of muscles, joints and other osteoligamentar structures is plausible, to the notion of chronic primary MSK pain, in which non-structural pathophysiological processes are incriminated [21, 27, 28].

Given that scientists and clinicians consider that chronic low back pain is mostly non-specific, which in the new ICD-11 classification was mechanistically referred to primary lumbar MSK pain, discussions and questions arise regarding the mechanisms underlying its base. The classification of chronic pain and the concept of primary versus secondary chronic pain were introduced in ICD-11 following the known classification principles used for headaches and other conditions, e.g., insomnia and hypertension, aiming to delineate these conditions for a management as well-argued and approved based on the recommendation grades [21]. Acquainting physicians with the principles of this classification will facilitate the training of patients in understanding that it is not peripheral factors that are largely responsible for pain, but central ones, on which treatment methods will be targeted [25].

An understanding of pain classifications is important when discussing musculoskeletal syndrome pain due to its variable presentation [29]. The group of authors who introduced the concept of chronic primary MSK pain claim that not all regional pain conditions are solely due to tissue abnormalities but that some aspects can be mechanistically explained as sensitization of the nervous system. It is suggested that chronic primary MSK pain, arising in muscles, tendons, bones, and joints in the absences of anatomical changes, is best understood as "regional fibromyalgia" [25].

There is room for debate as to what extent can the degenerative changes of the spine be considered as an unknown cause of low back pain. Possibly they can represent a causative factor, but which cannot be treated and diagnosed at the moment? It has been advocated that in approximately 90% of cases of low back pain a clear cause was not identified, although most times the advanced diagnostic techniques (e.g., diagnostic blocks or electrodiagnostic testing), while studying the etiological aspects of low back pain, were not used. At the same time, when they were visualized in different groups of people, it was observed that the respective changes did not cause pain in all cases. Shifting to the chronic stage of pain, this uncertainty increases, as lumbar pain tends to remain regionalized, but more diffuse, and to be associated with other manifestations, such as sensitization of the painful area with allodynia or hyperesthesia and other comorbidities (sleep disorders, cognitive problems, and others).

It is known that any chronic pain is supposed to be acute at the beginning, and every acute pain has a lesional substrate, with a potential mechanical triggering factor. In an attempt to understand the mechanisms of low back pain, so far there is no clarity in the use of the term of "non-specific" pain.

Chiarotto A. and the authors mention the uncertainty of the term non-specific pain, considering the fact that changes in the structures that can generate pain, such as muscles, intervertebral joints, intervertebral disc, cannot be confirmed by medical history and clinical examination. For example, osteoarthritis of the intervertebral joints can undergo the same inflammatory changes as the joints of another level, but until now there are no diagnostic criteria for vertebral osteoarthritis [28].

Among the causes of non-specific LBP, myofascial syndrome is considered one of the most common, being named as regional myofascial pain, which does not have any neuroanatomical distribution [25]. Evolving to chronic low back pain the central pain processing mechanisms are incriminated to be responsible for pain in absence of clear origin of nociceptive tissue damage, resulting in nociplastic pain. Nociplastic pain is distinct from nociceptive and neuropathic pain, in which central sensitisation has been found to be present in many subgroups of patients [12]. Clinical criteria proposed by Kosek E. et al. to identify nociplastic pain provide an opportunity to establish the possible or probable diagnosis.

Comparing the old concept of myofascial pain syndrome and the new concept of musculoskeletal pain, the question arises whether it refers to primary or secondary chronic MSK pain. Scientific research data, including experimental ones on animals, are presented about the fact that repeated mild trauma to muscle tissue and fascia by intramuscular injection of a small amount of nerve growth factor induces central sensitization of spinal neurons through neuron-glia interactions and neuroinflammation [22]. The author discusses whether the myofascial syndrome is a primary or secondary chronic pain and suggests completing the proposed classification with the third component "chronic myofascial pain" which would emphasize the possibility of the existence of the somatic factor (muscles, fascia) in the primary MSK pain. This concept would broaden the understanding of the biopsychosocial model of pain with emphasis on the neurobiology of muscle and fascia innervation and central nervous system signal processing.

The scientific debates on back pain are mostly related to terminology, which is observed from the stage of understanding low back pain as "non-specific" with nociceptive mechanism, in which the involvement of muscles, joints and other structures is plausible, to the notion of chronic primary MSK pain, in which non-structural central pathophysiological processes are incriminated, defined as nociplastic pain [21, 27, 28]. A research group that has been studying these conditions supports the idea that previous terms for the characterization of chronic pain, such as "idiopathic" or "functional" are inappropriate and even misleading and should have been modified. Contrary to this, they consider the use of the term nociplastic pain not suitable enough, as long as "centralized pain", central

sensitization, and central hypersensitivity are already widely used, terms that are much better understood by nonpain specialists [30]. According to Rolf-Detlef Treede who makes a critical analysis regarding the concept of chronic primary musculoskeletal pain, it is concluded that "The attempts to integrate the mechanistic concept of "nociplastic pain" and the older term "myofascial pain" are interesting, but the conclusions are premature without further empirical evidence" [21].

Conclusions

The term non-specific low back pain is used when the pain generators have not been accurately determined or if they have been mentioned, they cannot fully explain the existing symptomatology. At the same time, the denial of specific causative factors in these cases is premature since there are no objective methods of confirmation. Chronic primary musculoskeletal low back pain, in which nociceptive or neuropathic components are not observed, is better explained by central sensitization associated with biological and psychosocial mechanisms. Nociplastic pain as the third mechanistic description of pain was introduced; also, clinical criteria for possible or probable diagnosis were proposed. The introduction of the concept of chronic primary MSK pain has raised ambiguities and has sparked debate over its terminology and understanding. The need for further studies is outlined in order to capitalize and appreciate the role of myofascial structures in chronic low back pain.

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Authors' ORCID iDs and academic degrees
Svetlana Plesca, MD, PhD, Associate Professor – https://orcid.org/0000-0002-8141-3725
Oxana Grosu, MD, PhD, Scientific Researcher – https://orcid.org/0000-0002-8677-372X
Marina Sangheli, MD, PhD, Associate Professor – https://orcid.org/0000-0003-4064-9472

Authors' contributions
SP, OG, designed the research, drafted the manuscript and interpreted the data; MS revised the manuscript critically. All the authors revised and approved the final version of the manuscript.

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No competing interests were disclosed.