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EDITORIAL

Nociplastic pain: challenges and future perspectives

Dor nociplástica: desafios e perspectivas futuras

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For many years, different types of pain were classified as nociceptive based on the presence of an actual tissue injury or a threat to non-neural tissue that activated nociceptors. Pain that did not fall into this category was classified as neuropathic, defined as "pain initiated or caused by primary injury or dysfunction in the nervous system"[1]. In 2011, the updated definition of neuropathic pain was changed to "pain caused by injury or disease of the somatosensory nervous system"[1]. The change caused a gap in the classification of certain clinical conditions that did not show "activation of nociceptors" or "lesion or disease of the somatosensory nervous system"[2]. These conditions were characterized by alterations in the nociceptive system with widespread pain, without signs of injury or disease of the somatosensory system, with the presence of hypersensitivity even in apparently normal tissues.

On the other hand, the adoption of a term such as "idiopathic pain" could contribute to the stigmatization of these patients[1,3]. Therefore, a task force of the International Association for the Study of Pain (IASP) proposed the term "nociplastic pain" to include those conditions that did not fit into the classification of nociceptive or neuropathic pain[2]. This editorial seeks to present the historical evolution of this term and discuss the current challenges for clinicians and researchers.

Alterations in the nociceptive system, without consistent evidence of injury or disease in the somatosensory system, can be attributed to structural and functional changes in the central nervous system, including central sensitization (CS)[4]. The first proposals to include the term CS in a group of clinical conditions emerged in 2010[5,6]. Reference studies[6,7] presented, through a consensus of experts, a structured approach that listed clinical criteria suggesting nociceptive, peripheral neuropathic and central sensitization mechanisms for musculoskeletal pain. In 2014, another study[8] presented a flowchart for the classification of people with CS based on the following mandatory criteria: (i) exclusion of neuropathic pain and (ii) pain intensity disproportionate to the supposed source of nociception. When neuropathic pain is not present and the pain is considered to be of a disproportionate nature, at least one of the following criteria must be present: (i) diffuse distribution of pain and (ii) a score of 40 or more on the Central Sensitization Inventory (CSI).

Considering that CS is a neurophysiological mechanism and not a descriptor for the classification of pain, in 2016 the IASP adopted the term "nociplastic pain" as a third descriptor. This term, derived from "nociceptive plasticity", reflects changes in nociceptive pathways[2]. Nociplastic pain is defined as "pain that arises from altered nociception, despite there being no clear evidence of actual tissue damage or threat causing the activation of peripheral nociceptors or evidence of disease or injury to the somatosensory system causing the pain". In 2021, the IASP presented the classification system for nociplastic pain involving the musculoskeletal system[9].

These criteria consider that for patients to be classified with "possible nociplastic pain" they must: (i) report pain lasting for at least 3 months; (ii) report a regional distribution of pain rather than discrete; (iii) report pain that cannot be entirely explained by nociceptive or neuropathic mechanisms; (iv) show clinical signs of hypersensitivity to pain. In order to be classified as "possible nociplastic pain", in addition to the 4 criteria described above, patients must present: (i) a history of painful hypersensitivity in the area of pain, i.e. sensitivity to touch, movement, pressure or heat/cold; and (ii) at least one of the comorbidities: sensitivity to sound, light and/or odors, sleep disturbance, fatigue or cognitive problems[9].

The significant advances in terminology, definitions and clinical criteria are recognized. However, significant limitations and challenges remain. The use of the phenotype-based classification term is considered more appropriate than mechanism-based classification. The justification is that phenotype refers to observable or measurable characteristics and, to date, the precise mechanisms of nociplastic pain have not been fully clarified, suggesting that the term "nociplastic" does not reflect a neurophysiological mechanism.

There are still no "reference standard" tests to properly identify nociplastic pain. Another point that can cause confusion is the assumption that nociplastic pain is a synonym or underlying mechanism for primary chronic pain (PCP) (MG30.0), which is included in the International Classification of Diseases (ICD-11).

PCP is a concept aimed at classifying and recognizing a group of painful clinical conditions as a disease. Nociplastic pain is not included in the PCP definition and should therefore be understood as a descriptor of pain characteristics, rather than a diagnostic entity. Furthermore, current classification systems for nociplastic pain have only been suggested for the musculoskeletal system and should not be extrapolated to other conditions such as headaches, abdominal and pelvic pain.

It should be noted that the development of criteria for pain classification based on phenotypes is constantly evolving. In order to move towards the clinical implementation of this classification, research must establish the validity, usefulness, reliability and diagnostic accuracy of these criteria[10]. Research should identify whether certain characteristics are specific to a given pain phenotype. Studies should provide eviden-

ce on prognostic value and state whether treatments based on pain phenotype are more effective or not. Taking these gaps into consideration, clinicians should be careful when implementing the current nociplastic pain classification system and recognize the limitations and variability of pain characteristics with the possibility of patients not fitting into any of the three classifications, having overlapping characteristics, or features that change over time.

Yours sincerely,

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