## Pain beyond the brain-centered paradigm

A dor para além do paradigma cérebro-centrado

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The experience of pain can be challenging, not least because of its ambiguity. On the one hand, acute pain is a symptom that motivates a change in behavior to protect the individual. On the other hand, chronic pain, which can be a disease in itself, associated with disability, loss of functionality and suffering. The complexity of pain transcends the peripheral cause (injury) and the central cause (brain interpretation).

Pain is recognized as a disease by the International Classification of Diseases (ICD 11), but it can be classified into seven different categories, which complements its intriguing clinical and scientific definition<sup>1</sup>. This diversity of diagnostic codes can be seen as further evidence of the multidimensional complexity that health professionals need to address in order to understand and treat pain. Despite the expansion of multimodal and multiprofessional therapeutic options, the prevalence and social impact of pain remain almost unchanged. Pain, as a disease, can persist even in the absence of indicators of peripheral damage. Although the brain plays a central role in the perception of pain, the complexity of the phenomenon spills over into the interaction between elements emerging from social, cultural, psychological, emotional and contextual factors. The study of pain transcends the brain, medicine, the health sciences and the humanities.

Initially described from the Cartesian model perspective, pain was attributed to a specific cause, such as tissue damage. This linear model, proposed by René Descartes in the 17th century, did not consider pain modulation mechanisms, i.e. it disregarded interpersonal differences in the perception of pain. However, since the mid-20th century, the paradigm has been reformulated and pain has come to be investigated and understood from a multidimensional perspective.

With the advent of cognitive neuroscience came the tendency to analyze pain from a brain-centered perspective<sup>2</sup>. In this view, nociception would be "dissociated" from pain and the brain's interpretive response would be directly dependent on the perceived threat value. Despite the concept being supported by cognitive neuroscience, some authors question the tendency towards reductionism and simplification of the complexity surrounding pain itself. To limit the multidimensionality of pain to the mechanism of the central organ is, in a way, to minimize - or even neglect - the importance of the peripheral system in the perception of the symptom. Wouldn't we be oversimplifying the complexity of pain? The aim of this editorial is to rethink the brain-centered perspective of pain, highlighting its limitations and exploring the understanding of more complex approaches. Pain is not just a sensation or an experience and would perhaps be better understood if it were attributed to the emergent properties of the interactions of the complex pain, but also encompasses biology from an epistemological point of view, with the foundations and methods of scientific knowledge.

The dichotomous discourse of pain as a top-down or bottom-up process should not be exclusive and, more importantly, the pain process should not be seen as a direct process. There are fundamental contributions from peripheral mechanisms in the cortical reorganization, production and maintenance of pain.

Although the involvement of peripheral mechanisms in complex pain syndromes - such as phantom limb pain and fibromyalgia - is poorly understood, it is important to consider peripheral contributions beyond the brain-centered perspective<sup>3</sup>. In the treatment of pain, peripherally acting therapeutic approaches have an attenuating effect, albeit short-term, providing mild to moderate relief in pain intensity. Similarly, centrally-acting approaches have their relieving effects, which are also limited in terms of duration and reduction in intensity, with emphasis on the side effects of centrally-acting drugs, which affect cognitive functions, attention levels and cause drowsiness, among other effects<sup>4</sup>. To a certain extent, there is a consensus that approaches with exclusively central or peripheral action tend to have a limited therapeutic effect compared to multimodal approaches.

The growing trend towards a diversity of therapeutic options should not be taken to mean that any one of them can be effective on its own, whether they are new drugs, a combination of drugs, minimally invasive procedures, pain education programs, treatment with cognitive-behavioral therapy or other similar techniques, exercise prescription, functional and work movement re-education with energy-saving techniques, mindfulness or interactive therapies. Pain treatment requires complex approaches, so it must not neglect the dimensions of biomedical, biological, peripheral, central, psycho-emotional, socio-cultural and contextual knowledge, without losing sight of the multidimensional complex model.

It's time to adapt pain treatment. Evidence supports protective factors and places the therapeutic focus on chronic pain treatment that requires the patient's active participation in changing habits: quality of sleep, diet, job satisfaction and physical activity. The treatment of pain itself requires an increase in the perception of self-efficacy and pain control (pharmacological and other approaches) to enable



the person with chronic pain to give their pain a new meaning, promote changes in their quality of life and rebuild their social role, both emotionally and economically<sup>5,6</sup>. This complex scenario would perhaps be the starting point for changing the social, family and personal burden that people with chronic illnesses face.

From the point of view of scientific publication, rigorous argumentation is necessary to avoid analyses with reductionist tendencies. Therapeutic approaches and neurophysiological mechanisms have effects that depend on interactions between dynamic systems. Just as Melzalck<sup>2</sup> pointed out that the cortical neuromatrix theory was not limited to pain, the relativistic brain theory<sup>7</sup> also permeates the complexity of motor control and the understanding of variability in pain perception. This understanding considers that behavioral responses are influenced by the interaction of system elements and that these elements are not always computable, treatable or predictable.

Despite the comprehensive understanding of pain, single-factorial research studies remain necessary to build knowledge, while recognizing that the action of a single strategy or a single element is limited in the face of the system. Although isolated approaches report limited effects, they encourage multifactorial combinations to enhance the therapeutic effect. For example, the prescription of physical exercise is essential for a multidisciplinary chronic pain program. Despite the high evidence of effect, the person with pain may need medication before starting exercise, because with the partial pain relief provided by the medication they feel comfortable enough to face the exercises. In this multi-professional work, discussion between the parties is essential, as some pain-relieving drugs also influence the latency of muscle contraction, which can impair performance. In addition, some medications reduce the level of consciousness and can impair motor control and psychomotor balance skills, increasing the risk of falls in simple activities such as walking.

The complexity of pain transcends the brain, it is not limited to a creation of the mind or body, and its experience is connected to human suffering. Pain irritates, modifies emotions and impairs concentration and motivation. The challenge presented here requires that, in addition to objective, quantitative and standardized variables, science and the clinical approach recognize pain as an individual experience, without demonizing it or devaluing the intuitive and emotional aspects associated with it. Questioning the brain-centered perspective is not to detract from its value, but to emphasize that it is perhaps just one piece in the puzzle of understanding and treating pain.

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