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Literature review

# Cognitive and affective neuroscience of chronic pain: relevance for physiotherapy

# Neurociência cognitiva e afetiva em dor crônica: relevância para a fisioterapia

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**Resumo | Introdução:** A dor crônica é o principal motivo das consultas médicas, bem como um dos principais encargos para o sistema de saúde nos países desenvolvidos. No entanto, as terapias atuais ainda são inadequadas para certos tipos de dor crônica, como no caso da fibromialgia, ou causam efeitos colaterais intoleráveis (como opióides). Compreender as bases neurofisiológicas e psicobiológicas da dor crônica é crucial para desenvolver estratégias adequadas e eficientes para avaliação e tratamento multidisciplinar da dor. **Objetivo:** O objetivo deste trabalho é fornecer um breve resumo do estado atual da arte para esclarecer as estratégias mais eficazes para o tratamento da dor crônica. **Métodos:** Revisão narrativa da literatura desenvolvido em um centro mundial de referência para estudar a dor crônica. **Resultados:** Nas últimas décadas foi demonstrado que as mudanças plásticas que ocorrem no cérebro são fundamentais para a compreensão da manutenção da dor ao longo do tempo. As pesquisas forneceram evidências de que pacientes com dor crônica apresentaram processamento cerebral anormal da informação corporal e que estados emocionais negativos podem alterar significativamente o funcionamento do cérebro e amplificar o sofrimento associado à dor. Por outro lado, sugeriu-se que o fortalecimento das habilidades de regulação emocional através da reavaliação cognitiva e supressão, como usado na terapia cognitivo-comportamental ou na atenção plena, pode ajudar a regular a dor e a emoção em pacientes com dor crônica. No entanto, os mecanismos cerebrais envolvidos nestes processos regulatórios ainda devem ser elucidados, antes de serem transferidos para a prática clínica. **Conclusão:** A neurociência cognitiva e afetiva é fundamental para a compreensão da dor crônica.

**Palavras chave:** Dor crônica. Neurociência. Comportamento.

**Abstract | Background:** Chronic pain is the main reason for medical consultation, as well as one of the main burdens of the health system in the developed world. However, current therapies are still inadequate for certain types of chronic pain, as in the case of fibromyalgia syndrome, or cause intolerable side effects (such as opioids). Understanding the neurophysiological and psychobiological bases of chronic pain is crucial to develop adequate and efficient strategies for the multidisciplinary evaluation and treatment of pain. **Objective:** The aim of this work is to provide a brief summary of the current state of the art to clarify the most effective strategies for the treatment of chronic pain. **Methods:** Narrative literature study developed in a reference world center to study of chronic pain. **Results:** In the last decades, it has been demonstrated that the plastic changes that occur in the brain are key for understanding the maintenance of pain over time. Research has provided evidence that patients with chronic pain displayed abnormal brain processing of body information and that negative emotional states can significantly alter brain functioning and amplify the suffering associated with pain. On the other hand, it has been suggested that strengthening emotional regulation skills through cognitive reassessment and suppression as used in cognitive-behavioral therapy or mindfulness can help regulate pain and emotion in patients with chronic pain. However, the brain mechanisms involved in these regulatory processes must still be elucidated, before being transferred to clinical practice. **Conclusion:** Cognitive and affective neuroscience is fundamental to physiotherapists understanding chronic pain.

**Keywords:** Chronic Pain. Neuroscience. Behavior.

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## Introduction

Pain is a well-known subjective, sensory and affective experience elicited by the central nervous system. From a very restrictive perspective, pain is a psychobiological response to body injury and represents a symptom of illness. Nevertheless, pain has positive consequences for the organism since it triggers physiological and psychological reactions directed towards the recovery of body functions and survival. From this adaptive perspective, pain fulfills three relevant functions: alarm, recovery and communication. The experience of pain serves as a warning signal to indicate the existence of bodily harm in the individual. The measurement of pain and other vital signs provides relevant information on the correct functioning of the body and, therefore, any alteration in the critical levels of these vital signs are indicators of the integrity of the organism. The main problem that pain presents as a vital sign is probably the difficulty of measuring it objectively in the clinical setting. It must be taken into account that pain is, fundamentally, a subjective experience. In recent years, neuroscience research is providing new tools to objectively record pain in humans.

Moreover, the possibility of perceiving and experiencing pain allows organisms to initiate appropriate behavior to repair bodily harm. In this sense, the subjective experience of pain has physiological characteristics similar to other subjective sensations such as hunger, thirst or cold / heat. Thus, for example, pain experience elicits typical behaviors to reduce bodily injury and to facilitate recovery (for instance, resting, massaging of the injured area, taking of analgesics, expressing anger, preventing bad postures, praying or complaining). Additionally, facial and verbal expression of pain fulfills an important function of social human communication, allowing individuals who share the same culture to successfully understand and interpret pain in others. The experience of pain usually triggers a facial expression characterized by the lowering and constriction of the eyebrows, the lifting of the cheeks, the reduction of the opening of the eyelids until closing of the eyes, the wrinkling of the nose, the descent of the jaw and the opening of the mouth. In this way, the facial expression of pain, as occurs with the facial expression of other emotions (happiness, sadness, anger, fear, etc.), is characterized by a typical muscle activation pattern that is usually interpreted appropriately by most individuals. In addition, patterns of pain self-expression and pain recognition contain components similar to those of other emotional expressions: verbal (moans, screaming, etc.), motors (changes in posture, facial expression) and physiological (sweating, changes in vascularization of the skin and cardiovascular activity, etc.).

As stated by the International Association for the Study of Pain, pain should be defined as an unpleasant sensory and emotional experience associated with bodily harm that may be real or described in those terms (International Association for the Study of Pain). As a consequence, the clinical assessment of pain must include an evaluation of all these aspects, including an evaluation of brain function.

From a neurophysiological point of view, pain is defined as a subjective experience originated by the arrival of nociceptive information to the central nervous system, involving different brain regions intervene. The functions performed by these regions are related to different processes or psychological functions that accompany pain. Thus, for example, when an injury occurs in the body, the degree of itching, burning or swelling can be perceived, but it is also possible to locate the exact origin of this sensation in the body and estimate its duration and intensity. In addition, it is possible that the painful sensation attracts all the attention, that pain makes difficult to be distracted by other activities, that pain changes mood, that facial expression becomes more rigid, that daily activity is reduced and that the patient search the consolation of other people (doctor, family, social care, etc.). All these examples illustrate the idea that pain perception goes beyond a mere bodily sensation, but also that pain is a biological function that is accompanied by multiple psychological factors such as emotions, attention or memory. Nowadays, it is known that a wide network of cerebral structures, including somatosensory cortices, cingulate gyrus, prefrontal cortex, basal ganglia or periaqueductal gray matter, triggers activation of all these psychological processes or factors during the experience of pain.

## Chronic pain

The experience of pain is usually limited in time, since it is likely that the activation of the nociceptive system finally disappears with the healing process. Sometimes, however, pain goes on excessively over time, stops fulfilling an adaptive function and becomes a health problem on a personal and social level. In these cases, pain usually persists for months or even years after the damage to the body has been repaired, thus becoming a source of continuous suffering and conditioning patient's whole life. Therefore, when pain persists over time it stops being a symptom of bodily harm to become a disease. From a clinical point of view, the chronification of pain implies important changes in the life of the individual that affects both the emotional, cognitive and social status, as well as brain functioning. According to the International Association for the Study of Pain, pain is considered chronic when it is sustained for more than 6 months. Chronic pain is a complex phenomenon that goes beyond the prolongation in time of an unpleasant sensation associated with bodily harm. Furthermore, chronic pain is a major health problem that is due to the associated disability and the difficulty of applying an effective treatment, but mainly due to its high prevalence among the adult population.

There is currently abundant clinical and empirical evidence on the differences that distinguish acute pain from chronic or pathological pain. These differences also support the idea that evaluation techniques and the therapeutic approach that is effective in the case of acute pain, may not be suitable for chronic pain. First, people with chronic pain show a lack of correspondence between the magnitude of the bodily harm and the subjective intensity of pain they perceive. In general, the subjective perception that our senses give us (sight, hearing, taste, smell, touch, etc.) is related to the physical magnitude of the stimuli we perceive. However, in the case of chronic pain there seems to be a disproportionate relationship between the bodily harm and the intensity of the perceived pain.

Despite the relevance of the problem and the knowledge acquired during the last years, the clinical evaluation and the therapeutic treatment of chronic pain are still in development. In this regard, it is remarkable that a report of the British Pain Society published in 2009, noted that clinical training on the identification, assessment and treatment of pain in universities in the United Kingdom represents only 1% of the total training received by health professionals (http://www.britishpainsociety.org/media_surveys.htm).

## Pain in the brain

Neuroscience research in recent decades has repeatedly shown that the experience of pain is associated with the activation of a brain network formed by various structures. This network would be composed of brain regions that are necessary to obtain a complete pain experience. In this sense, it has been demonstrated that different structures could be responsible for the different components (sensory, affective, cognitive, motivational) that make up the complex experience of pain. On the other hand, research on chronic pain has revealed that the persistence of pain over time is associated with certain functional and structural changes of the CNS[1]. Current scientific evidence also suggests that the chronification of pain causes significant alterations in brain function and that therapeutic interventions should be developed to minimize and reduce the long-term effects of pain. The work of our research group is based on the hypothesis that brain alterations presented by patients with chronic pain can modify the processing of sensory, emotional and cognitive information related to bread. In summary, it is very likely that the development and maintenance of pain over time leads to the formation of a fingerprint or memory in the brain that is responsible, in turn, for a pattern of neurophysiological activity that maintains pain in the brain.

But, how is pain processed in healthy individuals? Studies using neuroimaging techniques (functional magnetic resonance and positron emission tomography) have found that responses to pain include changes in regional blood flow and oxygen consumption in brain structures such as somatosensory cortices (primary and secondary), the anterior cingulate gyrus, the insula, the thalamus, the posterior parietal cortex and the prefrontal cortex. The increase in activity on somatosensory cortices and insula has been related to the ability to discriminate the intensity of painful stimuli[2]. Increased activation in anterior cingulate cortex seems to be related to psychogical psychological factors suchs as the affective-motivational component of pain[3], as well as to cognitive and attentional responses to pain stimuli[4] and pain anticipaton[5]. Finally, the dorsolateral prefrontal cortex and the posterior parietal cortex appear to be involved in the processing of pain by their mediation in the cognitive aspects associated with the location and complete coding of the painful stimulus6.

**Chronic pain and CNS hyperexcitability**

The study of chronic pain has revealed that although initially pain has its origin in a specific pathological process, it represents a different nosological entity characterized by altered perceptual phenomena such as allodynia and hyperalgesia. One of the most discussed neurobiological mechanism regarding chronic pain is the sensitization or hyperexcitability of the nervous system. Thus, for example, it has been observed that trauma or bodily harm may lead to significant changes in the biochemistry and neural connections of the spinal cord and the brain[7]. Moreover, it has been repeatedly observed that patients with chronic pain have an altered brain functioning together with an enhanced pain sensitivity. Several studies have shown that patients with chronic pain have a greater sensitivity to mechanical or thermal stimuli than healthy people[8,9,10]. It has also been shown that this increased sensitivity for pain can be generalized to the entire body and is not limited to the damaged body area. In recent years, studies using neuroimaging techniques further demonstrated that pain stimulation may elicit opposite brain responses in different types of chronic pain. Thus, for instance, painful thermal stimuli seem to trigger reduced brain activity in regions generally involved in pain processing (anterior cingulate cortex, medial and orbitofrontal prefrontal cortex) in patients with pain due to rheumatoid arthritis. On the other hand, patients with complex regional syndrome or chronic mechanical back pain may have a brain response similar to that shown by healthy people. By contrast, patients with fibromyalgia show greater activity in different brain regions in response to painful and non-painful stimulation. Therefore, it appears that pain processing among patients suffering from different chronic pain syndromes may be subject to multiple factors that still need to be explored.

Our research has demonstrated that the chronic pain not only causes important changes on brain processing of stimuli that affect the body, but also on processing of emotions and cognition[1,8,11-29]. These results point to the existence of a pattern of cortical hyperexcitability in patients with chronic pain that could be modulated by emotional factors (depression, anxiety), cognitive (catastrophism) and social (perceived social support). All these studies have revealed that chronic pain might lead to relevant functional brain alterations both during the processing of painful and non-painful body information. Particularly noteworthy are the studies on alterations in brain networks associated with chronic pain during rest[11,12,16,28]. Thus, for instance, it has been shown that patients with fibromyalgia have a significant increase in the functional connectivity between the cingulate gyrus and the insula (both brain regions involved in pain processing), together with a significant reduction in the functional connectivity between the insula and the periaqueductal gray matter (involved in the modulatory and inhibitory pain)[12]. These studies have shown that the functional connectivity of patients with chronic pain displayed differential characteristics with respect to healthy volunteers even in the absence of any type of painful stimulation or task.

There are, however, some limitations that it should be born in mind when interpreting the results from neuroimaging studies of chronic pain. First, the elicitation of pain in lab settings is quite different from spontaneous and clinical pain perceived by patients with chronic pain. Secondly, it is necessary to take into account that chronic pain is related to specific psychological characteristics such as negative mood or negative thoughts (catastrophism, rumination, etc.) and, hence, these factors should be integrated into the analyses of brain activation to clarify their role for the maintenance of chronic pain. Thus, for example, it has been observed that patients with high levels of negative thoughts have greater activation of those brain regions involved in functions such as the anticipation of pain (medial frontal cortex, cerebellum), attention to pain (anterior cingulate gyrus, dorsolateral prefrontal cortex), the affective component of pain or motor control[30]. Therefore, all this requires the study of multidimensional factors that affect the perception of pain and its influence on brain activity in patients with chronic pain, as well as the study of the processing of spontaneous pain, without the application of painful stimulation.

Finally, given the high prevalence of chronic pain and its increase in adulthood, the influence of age on the cerebral processing of pain should be examined with greater rigor. In this sense, there are two types of empirical evidence that point to the modulating effect that age seems to play in the brain's processing of pain and that deserve special attention. On the one hand, the brain structures involved in the pain network appear to be differently activated depending on age. Thus, a recent study has found that brain activation (insula, cingulate gyrus or primary somatosensory cortex) triggered by the application of painful stimuli is lower in older people (around 80 years old) than in young people (between 18 and 30 years old). On the other hand, it was found that older adults have reductions in the amount of gray matter in brain regions such as insula and somatosensory cortex. All these findings suggest the possibility of a close relationship between the alteration in the cerebral response to pain, changes in pain sensitivity and the high prevalence of chronic pain in elderly patients.

### The role of physiotherapy and neuromodulation in chronic pain

As a result of these findings, much has been advanced in the search for a way to activate or inhibit cortical areas non-invasively in people with chronic pain31. Physiotherapy plays a fundamental role in neuromodulation since, because it is a profession that uses physical resources to treat human movement, its participation in the multidisciplinary team becomes essential. Through transcranial direct current stimulation and transcranial magnetic stimulation, this professional has developed fundamental research to understand the functioning of the brain in chronic pain, especially related to motor control. However, the complexity of the brain in chronic pain requires the interaction between professionals and researchers from different fields of knowledge.

## Conclusions

The activation of the brain pain network in patients with chronic pain does not depend only on the physical properties of the stimulation received (magnitude of the bodily harm that causes the pain). Empirical evidence has revealed that this pain-related brain network could become activated by affective (depression, anxiety), cognitive (attention, memory, etc.) and social factors (social support, sex, age) that are intrinsically involved in the experience of pain. It is already acknowledged that chronic pain exerts significant effects on the central nervous system which could be responsible for its maintenance over the time. Future multidisciplinary research should elucidate how the brain alterations caused by chronic pain and aging might contribute to the establishment and persistence of a memory for pain.

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**Competing interests**

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

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