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## Review Article

# Depressive disorder, anxiety disorder and chronic pain: Multiple manifestations of a common clinical and pathophysiological core<sup>☆</sup>

Cesar A. Arango-Dávila<sup>a,b,\*</sup>, Hernán G. Rincón-Hoyos<sup>a,c</sup>

<sup>a</sup> Sección de Psiquiatría y Psicología, Fundación Valle del Lili, Cali, Colombia

<sup>b</sup> Grupo de Investigación Biomédica, Universidad Icesi, Cali, Colombia

<sup>c</sup> Department of Psychiatry and Behavioral Sciences, Leonard M. Miller School of Medicine, University of Miami, Miami, United States

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## ABSTRACT

**Introduction:** A high proportion of depressive disorders are accompanied by anxious manifestations, just as depression and anxiety often present with many painful manifestations, or conversely, painful manifestations cause or worsen depressive and anxious expressions. There is increasingly more evidence of the pathophysiological, and neurophysiological and technical imaging similarity of pain and depression.

**Methods:** Narrative review of the pathophysiological and clinical aspects of depression and chronic pain comorbidity. Research articles are included that emphasise the most relevant elements related to understanding the pathophysiology of both manifestations.

**Results:** The pathological origin, physiology and clinical approach to these disorders have been more clearly established with the latest advances in biochemical and cellular techniques, as well as the advent of imaging technologies. This information is systematised with comprehensive images and clinical pictures.

**Conclusions:** The recognition that the polymorphism of inflammation-related genes generates susceptibility to depressive manifestations and may modify the response to antidepressant treatments establishes that the inflammatory response is not only an aetiopathogenic component of pain, but also of stress and depression. Likewise, the similarity in approach with images corroborates not only the structural, but the functional and pathophysiological analogy between depression and chronic pain. Knowledge of depression-anxiety-chronic pain comorbidity is essential in the search for effective therapeutic interventions.

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\* Corresponding author.

E-mail address: [arangodavila@gmail.com](mailto:arangodavila@gmail.com) (C.A. Arango-Dávila).

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## Trastorno depresivo, trastorno de ansiedad y dolor crónico: múltiples manifestaciones de un núcleo fisiopatológico y clínico común

### R E S U M E N

#### Palabras clave:

Ansiedad  
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**Introducción:** Una alta proporción de los trastornos depresivos se acompañan de manifestaciones ansiosas, así como la depresión y la ansiedad cursan frecuentemente con dolor. En otro sentido, las manifestaciones dolorosas causan o empeoran los síntomas depresivos y ansiosos. Cada vez hay más evidencia sobre la similitud fisiopatológica, imagenológica y neurofisiológica del dolor y la depresión.

**Métodos:** Revisión narrativa de los aspectos fisiopatológicos y clínicos de la comorbilidad depresión y dolor crónico. Se incluyen los artículos de investigación que enfatizan los elementos relevantes relacionados con la comprensión de la fisiopatología de ambas manifestaciones.

**Resultados:** Con los más recientes avances en técnicas bioquímicas y celulares y el advenimiento de tecnologías imagenológicas de avanzada, se ha podido considerar cada vez más claramente la aproximación etiopatogénica, fisiopatológica y clínica de estos trastornos. Se sistematiza esta información en imágenes y cuadros comprensivos.

**Conclusiones:** El reconocimiento de que el polimorfismo de los genes relacionados con la inflamación genera susceptibilidad a las manifestaciones depresivas y puede modificar la respuesta a los tratamientos antidepresivos establece que la respuesta inflamatoria no solo es un componente etiopatogénico del dolor, sino del estrés y la depresión. De igual manera, la similitud en la aproximación con imágenes corrobora la analogía no solo estructural, sino también funcional y fisiopatológica, entre la depresión y el dolor crónico. El conocimiento de la comorbilidad depresión-ansiedad-dolor crónico es importante en la búsqueda de intervenciones terapéuticas eficaces.

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## Introduction

In 1989, Hudson and Pope proposed that a number of chronic medical and psychiatric conditions may be part of a family of related disorders that share a common pathophysiology, referring to them as affective spectrum disorders.<sup>1</sup> These disorders share features such as depressive and anxiety symptoms, they often respond to antidepressants and they are frequently associated with clinical conditions with painful physical symptoms such as fibromyalgia, chronic fatigue syndrome, migraine, irritable bowel syndrome and premenstrual dysphoric disorder.<sup>2</sup>

In primary care, physical symptoms are a common reason for consultation, but the underlying reason is depression. More than 50% of patients with depression report somatic complaints and at least 60% of these symptoms are pain-related.<sup>3</sup> Consulting with physical complaints reduces recognition of depression and anxiety, as the primary care physicians assume that all physical symptoms are caused by an underlying medical condition.<sup>4</sup> Numerous complaints of pain are associated with greater severity of the depression, while more severe pain is predictive of poor prognosis for the treatment of the depression.<sup>1</sup> The aetiopathogenic relationship between depression and anxiety states, pain and somatic disorders has become increasingly clear, and this has reinforced the concept of affective spectrum disorders. Patients with fibromyalgia, for example, are twice as likely to suffer from other

psychiatric disorders, especially depression or anxiety, as patients without fibromyalgia.<sup>5</sup>

Different classification systems in psychiatry either do not include chronic pain among the symptoms of depression or give it scant relevance. This has led to generalised acceptance of the idea that depression has very little association with chronic pain.<sup>3</sup> Pain does not feature as a symptom of any mood or anxiety disorder, and complaints of depression are marginal in the list of required symptoms among criteria for chronic pain disorder. Recent medical research indicates that this separation in terms of disease classification and symptoms is not consistent with the clinical and neurobiological reality.<sup>5,6</sup>

## Methods

This article is the result of a narrative review of the pathophysiological and clinical aspects of the relationship between depression, anxiety and chronic pain. We included research articles that gave prominence to data on major depression and chronic pain comorbidity, extracting the most relevant elements relating to understanding of the pathophysiology of the two conditions. We organised the abundance of information into a comprehensive text and considered a common psychopathological outcome, depression-anxiety-pain, which we have formulated into figures and tables.

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