



## Psychiatric Comorbidities in Migraine: Pathophysiology and Clinical Management

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### Introduction

Migraine is a prevalent neurological disorder that is highly associated with psychiatric disturbances, such as depression, anxiety, bipolar affective disorders, post-traumatic stress disorders and sleep dysfunctions. For example, migraineurs are up to 4 times more likely to suffer from a major depressive disorder and up to 3 times more likely to be tackled by a bipolar spectrum disorder than healthy individuals. Psychiatric comorbidities are known to be associated with a negative migraine prognostic, since these disorders are related to stress responses that induce the process of chronification and increase the level of severity, causing worse outcomes and a major disability for the individual and, as a consequence, reducing quality of life.

### Objectives

This summary aims to correlate the co-occurrence of psychiatric disorders in individuals with episodic and chronic migraine, approaching the common pathophysiological mechanisms of both diseases to improve the clinical management of this type of patients.

### Methods

A narrative review of literature was performed based on research in PubMed database using the boolean operator “and” and the descriptors “migraine”, “psychiatric” and “comorbidities”. Filters were used to select only review articles and systematic reviews with full-text availability. 131 articles were obtained in the PubMed database, of which 10 were selected and 6 were used.

### Results

Most of the patients presented a co-occurrence of migraine and psychiatric disorders, instead of only migraine, demonstrating a bidirectional relationship. Furthermore, compared to migraineurs without psychiatric comorbidities, patients with those types of disorders reported a reduction in the response to acute pharmacological treatment. Sleep dysfunctions, stress, depressive and anxiety disorders alter the transmission of nociceptive stimulus from thalamus to the brain cortex by the modulation of neurotransmitters, causing exacerbated tonic cerebral discharges that acts in the chronification of episodic migraine. More specifically, acute stress induces the dysregulation of allostatic responses, provoking functional and structural brain alterations, leading to chronic migraine. Psychiatric disorders and migraine share common pathophysiological mechanisms, such as serotonergic dysfunction – since decreased plasma 5-HT predisposes increased cortical spreading depression, raising the sensibility of trigeminovascular paths that leads to headache pain – and HPA axis hyperactivity, with larger activation of the hippocampus, increasing emotional response to pain presented in migraine attacks and exacerbating anxious and depressive symptoms. The efficacy of tricyclic antidepressants (TCAs) in migraine treatment also indicate an association with depression. However, while high doses are needed to treat depressive symptoms, migraine prevention with TCAs is effective with low dosages, and induces fewer side effects. The new generation of antidepressants, the Selective Serotonin Reuptake Inhibitors, did not present the same effect on preventing migraine, being no better than placebo. Therefore, the results reported that different treatments for migraine and psychiatric disorders were a more efficacious option than monotherapy.

### Conclusions

Psychiatric comorbidities have been demonstrated to be common in migraineurs – specially the chronic type – since these disorders modulate physiological pathways associated with the chronification of episodic migraine. Distinct pathophysiological mechanisms – for example, HPA axis hyperactivity and serotonergic dysfunction – are related to migraine, depression, anxiety and other psychiatric disorders, possibly explaining the high prevalence of co-occurrence. The pharmacological management of these disturbances is still limited and studies indicate that monotherapy is not the most proper approach. Therefore, more research needs to be conducted to enable suitable and improved treatment for both conditions.

**Keywords:** Clinical Management; Migraine; Pathophysiology; Psychiatric Comorbidities.