



Review

Pharmacological Treatments of Sleep–Wake Disorders: Update 2023

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Abstract: Biological, environmental, behavioral, and social factors can influence sleep and lead to sleep disorders or diseases. Sleep disorders are common, numerous, and heterogeneous in terms of their etiology, pathogenesis, and symptomatology. The management of sleep–wake circadian disorders (SWCDs) includes education on sleep hygiene, behavioral strategies, psychotherapy (cognitive behavioral therapy (CBT), particularly), instrument-based treatments (i.e., positive airway pressure therapy, hypoglossal nerve stimulation), and pharmacotherapy. Depending on the disease, therapy varies and is executed sequentially or can be a combination of several forms of therapy. Drugs used for SWCDs include traditional sleep- or wake-promoting agents and chronotherapeutic agents. Recently, novel medications, which more precisely act on specific neurochemical systems (i.e., the orexin system) important for sleep and waking, are also increasingly being used. In this review, the pharmacotherapy of common sleep disorders (insomnia, sleep-related breathing disorder, central disorders of hypersomnolence, circadian rhythm sleep–wake disorders, parasomnias, and sleep-related movement disorders) embedded in the overall therapeutic concept of each disorder is presented. There is also an outlook on possible future pharmacotherapies.

Keywords: pharmacotherapy; sleep–wake disorders; hypersomnolence; restless legs; syndrome; parasomnias; sleep-related breathing disorders; insomnia; circadian disorders



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1. Introduction

There is a growing understanding of the neurobiology and functions of sleep and its effects on human health, including brain and mental health [1]. More than 1/3 of the global population reports sleep loss [2,3]. Insufficient or irregular sleep and sleep–wake disorders adversely affect human health in several dimensions, with both immediate effects such as sleepiness, impairment at work, or reduced psychosocial well-being as well as increased risk for (i.e.,) dementia, stroke, cardiovascular disorders, and depression [4–6].

There is also a high economic burden of sleep disorders. In a European study from 2010, the costs of disorders of the brain were calculated. The burden of sleep disorders was high and comparable with mental and neurological disorders [7], i.e., for narcolepsy, the direct and indirect costs reached €10,000 per patient, annually. Recently, several professional societies have aimed at increasing awareness, education, and research on sleep and moving healthcare policy towards healthy sleep [1,6,8].

The neurobiology of sleep and wakefulness is complex and includes not only wake- or sleep-promoting systems but also homeostatic, circadian, and motivational processes [9,10]. The neurobiology of sleep is beyond the scope of this review, and reference is made to the relevant literature.

Biological factors, environmental, behavioral, and social factors all can influence sleep. The individual may influence some of these factors, such as sleep times, sleep duration, or

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