

**SEROTONIN AND SLEEP: MOLECULAR, FUNCTIONAL AND CLINICAL ASPECTS**

Edited by J. M. Monti, S. R. Pandi-Perumal, B. L. Jacobs, and D. J. Nutt  
621 pp, \$219  
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SEROTONIN (5-HYDROXYTRYPTAMINE [5-HT]) IS ONE OF the oldest biologically active compounds on earth, preserved through at least 500 million years of evolution. Since its discovery in the 1940s in the mammalian intestinal mucosa and in the central nervous system, 5-HT has been shown to be involved in virtually all cognitive and behavioral human functions, and alterations in its neurochemistry have been implicated in the etiology of a plethora of neuropsychiatric disorders, such as schizophrenia, depression, anxiety, and Parkinson disease. Since the beginning, it appeared that 5-HT might have a role in sleep, but initial enthusiasm has been dampened because of the subtle effect demonstrated by this monoamine. Today, the interest in 5-HT in sleep research is going through a renaissance, thanks to the availability of highly selective serotonergic compounds and the urgent need for new sleep disorder treatments owing to the shortcomings of current ones. Notably, more than one-quarter of the US population report receiving insufficient sleep; 10% report having sleep disorders.<sup>1</sup> The market for pharmaceutical companies developing new drug treatments for these disorders is potentially worth billions of dollars. The serotonergic system and in particular the 5-HT<sub>2</sub> receptor subtypes have recently emerged as among the most promising targets in the search for effective and well-tolerated novel medications for treating primary and secondary sleep disorders.

*Serotonin and Sleep* provides an excellent review of current knowledge of the role of serotonin in the regulation of sleep and waking. The editors have already compiled other important works and are world-recognized experts in sleep research. Given the scarcity of similar monographs and the recent developments in serotonin research with reference to sleep and waking, this book is particularly timely and relevant. Moreover, the editors have put together contributions from well-respected scientists in the field. The book is exceptionally well organized into 6 distinct sections in appropriate sequence. The introductory chapter by Ursin effectively sets the scene, giving an overview of the way in which serotonin has been and is currently conceived to play a role in sleep. Indeed, Ursin charts the evolution in thinking that initially viewed serotonin as a sleep transmitter and

then as a waking transmitter before recognizing the complex role played by serotonergic neurotransmission in both processes.

The introductory section is followed by another comprising 3 anatomical chapters. The first 2 deal with the neuroanatomy of the dorsal and median raphe nuclei and their projections and differences. The third reviews current knowledge about the role of serotonergic modulation in the neuronal circuits involved in the circadian regulation of behavior.

The third section is dedicated to a comprehensive review of both the localization and molecular biology of serotonin receptors in the mammalian brain. In the first chapter Artigas et al review current knowledge about the distribution of 5-HT receptor subtypes in the prefrontal cortex of rats and human and nonhuman primates. Hannon and Hoyer then go on to explain the diversity of serotonin receptor types and subtypes, detailing the synaptic actions of each receptor type and reflecting on its specific involvement in the susceptibility to determined pathologies and its role as target for therapeutic relief from these conditions.

In the fourth section, the editors have collected 5 papers on the theme of electrophysiology of 5-HT neurons and the regulation of serotonin release. Notably, Jacobs and Fornal review a series of electrophysiological studies on the activity of the serotonergic neurons in the brains of cats. They conclude that there is a role for serotonin in the coordination of motor, autonomic, and sensory processes. This section also includes 2 chapters on the regulation of dorsal raphe neuronal activity across the sleep-wake cycle. Sakai claims that the suppression of dorsal raphe serotonergic neural discharge in rapid eye movement (REM) sleep is attributable to the inhibition of firing discharge of norepinephrine, histamine, and orexin neurons during sleep; Sinton dedicates an exhaustive chapter to the orexinergic system. However, Luppi et al support the idea that this suppression is instead a result of an increase of  $\gamma$ -aminobutyric acid (GABA) function attributable to an excitation of GABA neurons located both inside and outside the raphe. Even neuropeptides are involved in sleep-related inhibition of 5-HT neuronal activity, changing the strength of GABAergic and glutamatergic inputs to the dorsal raphe, as reported by Auerbach.

The fifth section comprises 9 chapters on the theme of regulation of behavior by serotonin receptors. The various

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5-HT receptor subtypes are singled out in different chapters. Pace-Schott looks at the effect of selective serotonin reuptake inhibitors on dreaming in individuals with and without depression and hypothesizes as to the connections between REM sleep, serotonin, and dreaming. Portas and Gronli consider the complex role of 5-HT<sub>1A/1B</sub> receptors in the regulation of sleep and waking. Agonists to these receptors increase wakefulness, decrease REM sleep, and are involved in the modulation of circadian rhythms affecting the suprachiasmatic nucleus and the pineal gland. Kitka and Bagdy discuss the 5-HT<sub>2A/C</sub> subtypes, which seem the most promising for the development of new drugs. Staner et al review current knowledge of the 5-HT<sub>3</sub> receptors, stimulation of which increases wakefulness and reduces slow-wave sleep. Thomas reviews 5-HT<sub>7</sub> and reports evidence for involvement of the 5-HT<sub>7</sub> receptor in the dorsal raphe in the mechanisms that control REM sleep and mood disorders. The use of serotonin mutant mice in the study of sleep/waking regulation is described by Adrien, providing evidence for a novel role for serotonin in these functions. This section ends with a discussion by Sanford et al of the regulatory role of 5-HT in arousal and alerting systems at brainstem and amygdalar sites.

The book concludes with 4 chapters on serotonin and its significance for clinical disorders and drug actions. In particular, Buchanon et al and Veasey suggest that serotonin neurons are involved in state-dependent control in respiratory modulation. Abnormalities in these neurons could be implicated in such clinical pathologies as sudden infant death syndrome, panic disorder, and obstructive sleep apnea. Argyropoulos et al consider the alteration of sleep in depression and the affects of antidepressants. Winokur and Kamath discuss schizophrenia, the alteration of sleep architecture, and the action of antipsychotic drugs on sleep, revealing a critical role for 5-HT<sub>2A</sub> and dopamine D2 receptors.

To summarize, the editors have succeeded in putting together an excellent and informative book in sleep medicine. Minor drawbacks are the inevitable overlapping of some chapters and the minimal use of color tables. In addition, some chapters on the thalamic-cortical function in sleep and the role of 5-HT in their modulation would have been welcomed. However, the authors are to be congratulated for providing thorough literature reviews as well as reporting their own work. The well-thought-out organization and consequent readability of *Serotonin and Sleep* makes it an excellent choice not only for sleep and 5-HT scientists but also for industrial pharmacologists and students interested in the pathophysiology of sleep and the serotonin system.

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1. 2005 sleep in America poll: summary of findings. National Sleep Foundation Web site. [http://www.sleepfoundation.org/sites/default/files/2005\\_summary\\_of\\_findings.pdf](http://www.sleepfoundation.org/sites/default/files/2005_summary_of_findings.pdf). March 2005. Accessibility verified October 22, 2009.

### ~~TREATING CHILD AND ADOLESCENT DEPRESSION~~

~~Edited by Joseph M. Rey and Boris Birmaher~~

~~360 pp, \$69.95~~

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~~ISBN 13: 978 0 7817 9569 2~~

~~ALTHOUGH PROFESSIONALS HAVE RECOGNIZED CLINICAL depression in children and adolescents for the past 40 years, treatment research has only recently begun to identify promising treatment regimens. The editors of *Treating Child and Adolescent Depression* have successfully provided a comprehensive summary of the relevant evidence base related to childhood depression, translated into practical and easily digested information. While the book spans a broad range of topics, including epidemiology, types of depression, clinical course, etiology, risk factors, and effect of depression on functioning, the focus is clearly on assessment and treatment. This information presented is useful for a wide range of clinical, research, and lay audiences, including experienced mental health clinicians, general practitioners, students new to the field, or concerned parents.~~

~~Strengths include the comprehensive coverage of various treatment approaches (medication, biological approaches, cognitive behavioral therapy, interpersonal psychotherapy, family therapy, dynamic psychotherapy, and complementary and alternative approaches) as well as the treatment of youth with varying degrees of illness severity, comorbid disorders (eg, developmental disabilities, chronic illnesses, substance abuse, or other psychiatric diagnoses), and life circumstances (eg, histories of grief, trauma, or immigrant status).~~

~~The book presents far more than a cursory review. Detailed information is provided related to the conceptual basis for treatment, suitability for a specific child, techniques and details regarding treatment components, and recommendations for identifying and treating common obstacles or adverse effects. The book likewise provides evidenced-based advice related to the successful engagement of families into treatment, liaison with schools, management of adverse effects, treatment-resistant depression, specific types of crises and emergencies, treatment in primary care settings, and prevention. With chapter authors from Australia, Canada, New Zealand, Turkey, the United Kingdom, and the United States, international differences are highlighted. Eminently practical for teachers and clinicians, the book contains many~~

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