

Body Clocks in Health and Disease

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INTRODUCTION TO CIRCADIAN CLOCKS

Overview of Circadian Timing

A frustration in the search for mechanisms and treatments for brain-based disorders and diseases is the complex and seemingly overlapping nature of symptoms and causes associated with clinically defined states of health and illness. The circadian timing system, the subject of this chapter, is one of the system level mechanisms that impact an immense array of responses that either antecede or accompany diseases that claim the attention of neuroscientists. These include disturbed sleep/wake cycles and mood regulation, inappropriate food intake and metabolic factors that regulate fat and glucose metabolism and energy expenditure, and physiological responses including stress responses and the accompanying activation of hypothalamic–pituitary axes regulating hormone secretions. A growing body of evidence indicates that circadian “clocks” are located in most cells of the body and that they modulate functions that control emotional, cognitive, and metabolic processes, thereby pointing to mechanisms that can

link observed comorbidity in psychiatric and metabolic disruption. Additionally, polymorphisms in genes associated with the cell-based circadian clocks have been associated with sleep disorders and obesity.

Circadian rhythms can best be understood in the context in which they evolved. Living organisms on our planet have internal time-keeping systems, termed circadian “clocks” that enable anticipation of upcoming events for optimal timing of behavior, metabolism, and physiology with respect to predictable changes in the environment. At the level of a cell, system, and whole organism, each function of the body must find its appropriate temporal niche, as it is not possible to do everything all at once. While correlated with daily changes in day and night caused by the rotation of the earth about its axis, circadian rhythms are endogenously organized and are not dependent on timing signals from the environment. That is, even if all time cues are removed, such as occurs in deep underground caves or in outer space, circadian rhythms continue with a period of about 24 h.

One tremendous advantage in the analysis of circadian timing mechanisms is that research

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