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ARTICLES

[Pineal Melatonin: Cell Biology of Its Synthesis and of Its Physiological Interactions*](#)

[RUSSEL J. REITER](#)

- [Author Affiliations](#)

Department of Cellular and Structural Biology, The University of Texas Health Science Center at San Antonio San Antonio, Texas 78284-7762

Address requests for reprints to: Dr. Russel J. Reiter, Department of Cellular and Structural Biology, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78284-7762.

Abstract

I. Introduction UNTIL 35 yr ago, most scientists did not take research on the pineal gland seriously. The decade beginning in 1956, however, provided several discoveries that laid the foundation for what has become a very active area of investigation. These important early observations included the findings that, 1), the physiological activity of the pineal is influenced by the photoperiodic environment (1–5); 2), the gland contains a substance, *N*-acetyl-5-methoxytryptamine or melatonin, which has obvious endocrine capabilities (6, 7); 3), the function of the reproductive system in photoperiodically dependent rodents is inextricably linked to the physiology of the pineal gland (5, 8, 9); 4), the sympathetic innervation to the pineal is required for the gland to maintain its biosynthetic and endocrine activities (10, 11); and 5), the pineal gland can be rapidly removed from rodents with minimal damage to adjacent neural structures using a specially designed trephine (12).

Since the mid 1960s, research on the pineal gland has increased exponentially, and its association with a wide variety of physiological systems has been documented (13–18). Proof that melatonin is the hormone of pineal origin that accounts for many of the endocrine manifestations of the gland, however, came somewhat later. Thus, whereas some early studies certainly suggested that melatonin had modulatory effects on the neuroendocrine-reproductive axis (19, 20), these actions were questioned when it was observed that in hamsters bearing sc placed melatonin pellets, which release the indole continuously, the ability of short day exposure and the pineal to suppress reproductive physiology was unexpectedly negated (21–23). These observations were, however, followed closely by studies showing that melatonin, administered as a single daily injection at a precise time with regard to the light-dark cycle, induced quiescence of the neuroendocrine-reproductive axis just as did short day exposure (24, 25).

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This Article

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