Melatonin And The Mammalian Pineal Gland 1st Edition

Provides comprehensive, updated information on the structure, and cell and molecular biology of the vertebrate pineal organ, which is the source of the "timing hormone" melatonin.

There is considerable circumstantial evidence linking the pineal gland with schizophrenia. Moreover, the pineal hormone, melatonin and the enzyme, HIOMT, which facilitates the final stage in its biosynthesis, have been implicated in the disease. The present work set out to establish the possible potential role of pineal HIOMT in the biogenesis of schizophrenia. The localization of neuroleptic and hallucinogenic drugs in the pineal glands of rats together with isolated reports of the effects of other psychoactive drugs on pineal biochemistry suggested the possibility that the pineal might be a site of action. Consequently, biochemical studies were initiated to examine the effects of these drugs on pineal HIOMT activity. The neuroleptic drugs haloperidol and fluphenazine inhibited HIOMT "in vitro". Kinetic studies with haloperidol revealed that this inhibition was non-competitive in nature. It is suggested that this mechanism could be a possible mode of action of the antipsychotic drugs in schizophrenia. In addition, hallucinogenic compounds can produce symptoms in normal subjects which are often indistinguishable from schizophrenia. Studies with several hallucinogens revealed that these drugs activated the pineal enzyme, HIOMT,"in vitro". The balance of serotonin, dopamine and noradrenaline is thought to be important in maintaining normal behaviour. These experiments have led, therefore, to the hypothesis that the effects of psychoactive drugs might be mediated by their ability to interfere with melatonin synthesis and thus alter serotonin levels in the hypothalamus and midbrain. The possibility of pineal HI0MT facilitating abnormal transmethylations has been investigated. The enzyme was found to act on alternative substrates "in vitro" to yield N-acety]-3,4-dimethoxy-phenylethylamine (NADMPE), a compound which has been linked with causal factors in schizophrenia. Pigmentation effects have also been associated with schizophrenia, both through the oxidases which catalyse the formation of melanin and by way of melatonin, the most powerful skin lightening agent known. The possibility that melanin formation itself or melatonin synthesis might be modified at the molecular level by catecholamine/indole complex formation was also investigated. Kinetic studies of the inhibition of the tyrosinase catalysed oxidation of dopamine and L-DOPA by hydroxyindoles have shown that this was.

Melatonin is a hormonal signal for the photoperiod and is intricately involved in many aspects of circadian and seasonal physiology. This idoleamine is synthesized in the pineal gland and retinas of many vertebrate species. In mammals, melatonin of pineal origin is synthesized in pinealocytes that receive photic information indirectly via the retina, brain, and sympathetic nervous system. In many non-mammalian vertebrates, the hormone-producing cells of the pineal organ are the directly light-sensitive, pineal photoreceptors. This publication contains state-of-the-art approaches to the study of pinealocytes, including confocal microscopy with three-dimensional reconstruction, calcium imaging of identified cells, patch-clamp analysis of novel ion channels, and new techniques for the monitoring of circadian melatonin production. Moreover, recent findings on the molecular and pharmacological characteristics of melatonin receptors, mechanisms of melatonin action and human melatonin in health and disease are reviewed. This collection of papers offers a valuable resource in the study of circadian and seasonal physiology. It provides stimulating reading for chronobiologists, cell biologists, physiologists, pharmacologists, neuroendocrinologists, and other medical and biological researchers.

This volume contains the written contributions to the proceedings of a workshop related to the pineal gland and its hormones, which was held in Erice, Italy, on June 7 -June 13, 1994. This series of workshops, which began in 1982 and which have been held at four-year intervals since that time, has provided important continuity for advancing the state of knowledge relating to this very important investigative area. The enthusiasm for these conferences has increased steadily, as reflected in the number of individuals applying to attend and in the input of individuals who participate in the meeting. The 1994 meeting was important because of its timeliness. In the two years preceding the meeting a number of revolutionary discoveries were made relative to the actions of the pineal hormone melatonin. The Xenopus melatonin receptor was cloned, melatonin was demonstrated to be a potent antioxidant, the significance of melatonin receptors at the level of pars tuberalis in the regulation of the hypothalamo-pituitary-gonadal axis was questioned, a number of melatonin receptor analogues were discovered and successfully utilized, the mechanisms by which melatonin retards initiation and promotion of cancer was further elucidated, the clinical aspects of the pineal gland was re-scrutinized. Reviews relating to each of these subjects, as well as many others, are contained in this proceedings book. This volume represents an up-to-date repository for the most recent information related to this rapidly advancing field.

In this volume, current knowledge on light as a regulator of biological rhythms is considered from both basic science and clinical perspectives. Chapters by leading experts cover the whole range of biological rhythms, from infradian and circadian to the longer ultradian rhythms, in a wide variety of mammalian species. The chapters on humans provide a basis on which to establish mechanisms for mediating the therapeutic and physiologically beneficial effects of light as a regulator of rhythms in health and disease.

Structure and Function of the Epiphysis Cerebri

The pineal hormone melatonin is released following a circadian rhythm with high levels during the night and low levels during the day. Melatonin activates high affinity membrane receptors belonging to the G protein-coupled receptor superfamily. The mammalian MT1 and MT2 melatonin receptors are cloned and pharmacologically distinct. The temporal specificity through which melatonin mediates physiological responses will be dictated by the functional sensitivity of the MT1 and MT2 melatonin receptors. The overall goal of this thesis was to investigate melatonin-mediated desensitization of MT1 and MT2 melatonin receptors focusing on its physiological significance.

In the forty years since melatonin's isolation and characterization, a large and multifaceted database has accrued. This book documents the diverse research contributions of most of the major laboratories in the field of melatonin research, as presented in a special conference to mark the 40 year anniversary of the isolation and chemical identification of this hormone. In addition, many chapters by younger scientists provide an exciting glimpse of where melatonin research is heading in the future.

Melatonin (MEL) is a hormone secreted by the mammalian pineal gland in response to photoperiod and seasonal changes. In humans, the circadian rhythm of melatonin secretion is under the control of the circadian regulator in the suprachiasmatic nucleus of the hypothalamus. This indoleamine has been found in many organisms including plants. In plants, MEL has been detected in flowers, seeds, leaves, stems, and roots. It has been reported that MEL stimulates hypocotyl and root growth of lupin and Wisconsin Fast plants seedlings. In this study, the effect of exogenous MEL on the germination and development photo dormant tobacco seeds (Nicotiana tabacum cv. Havana) was investigated. The results indicate that MEL breaks photodormancy, accelerates germination rate, and promotes faster emergence of cotyledons. Changes during development associated with periodic addition of exogenous MEL revealed that MEL is a growth promoter in tobacco plants. From seedling stage all the way to flowering, MEL consistently affected tobacco growth and development. The MEL effects as a growth promoter were concentration dependent in some cases and not in others. Application of 10 pM MEL caused the most significant changes; tallest plants sometimes twice as tall as the control, the highest stem radial growth, the largest leaf size, and the earliest flowering. Treatments of 10 uM MEL slightly inhibited tobacco growth. At this MEL concentration tobacco plants never flowered. Melatonin is a good candidate to be elevated to a growth hormone status in tobacco plants with an effective concentration in the picomolar range.

This volume provides the reader with an overview of an intriguing and interdisciplinary field of research. For the first time the mammalian pineal gland, its mode of action and its physiological effects are discussed in a comprehensive, single-authored work.

It was only in the past few decades that we realized life is basically a coordinated interplay between cyclic biochemical processes in widely different forms and period of times. This recognition greatly altered our understanding on how living organisms function. The Avian Pineal Gland discusses one specific aspect of biological cycles: the mechanism of the circadian melatonin secretion from the chicken pineal gland. The plineal gland plays a key role in controlling circadian and seasonal rhythmic processes in virtually all vertebrate species. Also, the avian pineal gland is an excellent model for studying the mechanism of the circadian processes, since this organ is relatively simple in structure and it possesses all the known features of a fully functioning circadian biological clock.

Previous hypes and hopes have clouded the use of melatonin, the pineal gland indoleamine hormone, as a health food supplement. Recently however, significant advances have been made in our understanding of the signal transduction mechanisms of many well-known and potential physiological and pharmacological actions of melatonin in mammals. This timely publication was put together by an international group of pineal researchers whose major research focus is unraveling the mammalian physiology and pharmacology of melatonin at the cellular, tissue and organismic levels. It collates the latest scientific information on the receptor and non-receptor mediated mechanisms of melatonin actions. The respective articles address the roles played by G protein-coupled melatonin receptor subtypes in the modulation of biological rhythms in mammals, including the seasonal reproductive responses. The different functions of membrane and nuclear melatonin receptors in the regulation of mammalian immune responses and epididymal cell biology are also discussed. In addition, the biochemical mechanisms of the free radical scavenging functions of melatonin, using physiological and pharmacological concentrations are authoritatively reviewed in the specific contributions of this publication.

Critical life history events such as breeding, migration and hibernation must take place in the correct environmental context to minimize deleterious consequences on survival and reproductive fitness. Neuroendocrine mechanisms synchronizing internal physiological states with extrinsic environmental cues are vital to timing life history events appropriately. Secretion of the pineal hormone melatonin is sensitive to light and temperature cues, which provides a physiological indicator of time of day and time of year for organisms. Melatonin influences seasonal reproduction in a variety of vertebrates, likely by altering the synthesis and/or release of reproductive neuropeptides in the brain. The neuropeptides arginine vasotocin and its mammalian homologue, arginine vasopressin, are well-known modulators of reproductive and sociosexual behavior across vertebrate taxa, and are likely targets of melatonin in the context of seasonal reproduction. There is extensive evidence that vasotocin/vasopressin innervation in the brain is subject to seasonal variation, and that this variation is frequently sexually dimorphic. However, evidence that melatonin directly modulates this important neuropeptide system is lacking. Melatonin receptor 1a (MT1 in mammals) may be responsible for mediating melatonin's influence on brain vasotocin, as it is known to regulate seasonal reproduction in a variety of vertebrates. In the present study, I asked whether melatonin influences brain vasotocin in male green treefrogs (Hyla cinerea), and compared the distribution of melatonin receptor 1a in the brain of green treefrogs between sexes and seasons. Adult male and female green treefrogs were collected from field sites in Louisiana during the summer breeding season. Summer animals were acclimated to lab conditions for 3 weeks, then euthanized and their brains collected. Winter animals were maintained in the lab for four months under incrementally changing photo-, thermo-, and hygroperiod regimes that mimicked the transition to winter in their natural habitat, followed by euthanasia and brain collection. A subset of winter males (Experiment 1) were implanted with melatonin-filled or blank silastic capsules for a period of one month prior to euthanasia and brain collection. Brains of these males were processed for vasotocin immunohistochemistry. I quantified AVT-ir cell number in Experiment 1 males in the nucleus accumbens (NAcc), amygdala and caudal striatum (AMG), preoptic area (POA), suprachaismatic nucleus (SCN), and ventral hypothalamus (VH). Melatonin did not influence brain vasotocin-ir cell number in any brain region. Brains from untreated summer and winter males and females were collected and processed for MT1 immunohistochemistry. MT1-ir cells were quantified in the NAcc, striatum (STR), AMG, POA, SCN, and VH. In all regions quantified, reproductively active males had significantly more MT1-ir cells than nonreproductive males. Within the summer breeding season, males had significantly more MT1-ir cells in the NAcc than did reproductively active females. In all other regions there was no significant difference in MT1-ir cell number between reproductively active males and females. Collectively, these data suggest that melatonin modulates vasotocin via MT1. These findings assist in elucidating the neuroendocrine mechanisms by which vertebrates integrate seasonal cues with physiology to correctly time critical life history events.

Pineal and Retinal Relationships presents the proceedings of the Symposium on Pineal and Retinal Relationships, held in Sarasota, Florida on May 3–5, 1985. This book looks at the features that the retina of the lateral eyes and the pineal organ share, including biochemical processes, photoreceptive structures, biorhythmic phenomena, and physiological functions. This text also discusses the general and complex concept of photoneuroendocrine systems. Organized into 27 chapters, this book starts with an overview of the basic features of retinal and pineal receptors. It then proceeds with a discussion of the environmental factors that vertebrates use as cue to synchronize their circannual and circadian rhythms by which they adjust their physiological, behavioral, and biochemical functions. Other chapters consider the melatonin synthesis in vertebrates, which allows them to sequence physiological events into closer temporal position with seasonal climatic changes. This book is a valuable resource to optometrist, neurologist, neurosurgeons, photobiologists, ophthalmologists, and eye care professionals.

The pineal gland has been a subject of interest and speculation for more than 2000 years. Greek anatomists were impressed by the ob servation that the pineal gland is an unpaired structure and they believed that it regulated the flow of thoughts. The philosopher Descartes proposed an important role for this organ in brain function. At the beginning of the 20th century experiments by several investi gators indicated that the pineal influenced sexual function and skin pigmentation and was also responsive to light signals. With the iso lation of melatonin from bovine pineal glands by Lerner and cowork ers in 1958 the modern era of pineal research was initiated. Within a few years the pathway for the biosynthesis of melatonin in the pineal was elucidated. Soon thereafter it was shown that the formation of melatonin was influenced by environmental lighting. Ana tomists found that the pineal was innervated by sympathetic nerves and that the gland had photoreceptor elements. It was also shown that the gonads were influenced by light via the pineal gland. Research on the pineal gland became of increasing interest to anatomists, bioche mists, pharmacologists and endocrinologists. With the expanding know ledge concerning the function of the pineal gland contributed by the wide variety of disciplines, it was thought that a study workshop would be timely.

This book, on the pineal hormone melatonin, is addressed to a wide non-cognizant and cognizant readership. The hormone appears to be involved in sleep onset and other functions associated with the body’s clock, the suprachiasmic nucleus. It is ubiquitous throughout both the animal and plant kingdoms and has a long evolutionary history as a hormone. Melatonin has a major role in the regulation of circadian rhythms in non-mammalian vertebrates and forms part of their control in mammals. The present text emphasizes the positive role of exogenously administered melatonin, and its synthetic derivatives, on disrupted circadian rhythm-related dysfunctions. This is effected by resetting the clock in jet lag sufferers and those with seasonal affective disorders, insomnia, and various neurological conditions.

The Novartis Foundation Series is a popular collection of the proceedings from Novartis Foundation Symposia, in which groups of leading scientists from a range of topics across biology, chemistry and medicine assembled to present papers and discuss results. The Novartis Foundation, originally known as the Ciba Foundation, is well known to scientists and clinicians around the world.

Melatonin: Biosynthesis, Physiological Effects, and Clinical Applications provides a thorough review of recent advances in major areas of melatonin research. The book is arranged in a logical sequence, beginning with the history of melatonin and then proceeding to cover its biochemistry and secretion, physiological effects, and clinical significance. New findings and current concepts are emphasized, and a significant amount of previously unpublished data are included. The book will be an important reference for neurobiologists, cell biologists, ophthalmologists, endocrinologists, neuroendocrinologists, reproductive biologists, psychiatrists, and other researchers and clinicians interested in melatonin.

Research related to the pineal gland has advanced rapidly in the last three decades since the discovery of its most important hormone, melatonin. This indoleamine has been shown to have a large variety of effects in the organism; the bulk of these actions were initially thought to relate the pineal gland to the reproductive and endocrine systems. It is now apparent, however, that the physiologic interactions of the pineal and its hormones far transcend its control of endocrine function. One field of pineal research that has developed rapidly within the last 5 years has been the demonstration of its relationship to the immune system. Since the pineal gland is part of the central nervous system, these observations generally fall in the category of neuroimmunology, an area that, in its own right, has received a great deal of attention in the last decade. Thus, a NATO Advanced Study Course entitled "Role of Melatonin and Pineal Pep tides in Neuroimmunomodulation" was convened in Erice, Sicily, on June 3-9, 1990. This book is a result of the scientific presentations given at the workshop. The contributions to the book include mini-review articles which summarized the presentations of the invited speakers as well as a selected number of brief communications where the subject matter was in line with the theme of the Advanced Study Course.

In photoperiodic mammals, the timing of seasonal breeding cycles depends on the pineal hormone melatonin, which acts via high affinity melatonin MT1 receptors expressed in the hypothalamus and/or pituitary gland. While changes in nocturnal melatonin synchronises the annual reproductive cycle, thyroid hormones are also permissively required for the expression of the cycle. Using Soay sheep as a model, we have now demonstrated that a switch from short to long photoperiod (summer cue) causes melatonin-responsive cells in the pars tuberalis (PT) of the pituitary to increase local production of TSH. This appears to act by retrograde diffusion on TSH-receptor-expressing ependymal cells in the adjacent mediobasal hypothalamus to activate expression of type II thyroid hormone deiodinase (DIO2). DIO2 increases biologically active hypothalamic tri-iodothyronine levels to initiate the summer neuroendocrine cascade. In an initial experiment, male Soay sheep under short photoperiod were treated with oTSH icv for 5 days, which activated DIO2 expression in the ependymal cells of the third ventricle, as with long photoperiod. More recently, short-day acclimatized sheep were treated with oTSH icv for 21 days; in this case the treatment caused significant regression of the testes compared with vehicle-treated controls. These data and recent findings in quail indicate that the TSH-expressing cells of the PT play an ancestral role in seasonal reproductive control in vertebrates.

Designed for researchers, physicians, and lay people interested in the topic, Melatonin in Health Promotion examines virtually all aspects of the multifunctional hormone melatonin, a subject of intense scientific research and general interest. Topics addressed include how melatonin is synthesized; possible harmful side effects; and the role this hormone plays in diseases such as epilepsy, Alzheimer's, and cancer.

Paperback. This book contains a state-of-the-art view of the field of pineal research. It focuses on the pineal itself as well as on its relationship to endocrine function and psychiatric disorder. The following issues are covered by experts in the field: regulation of the pineal gland and in particular its relationship to circadian rhythms, the role of the pineal gland in seasonal and non-seasonal reproduction, the role of the pineal gland in humans and mammalian physiology, abnormalities of the pineal gland in depressive illness, and brain targets for pineal actions.

This timely publication describes several newly identified functions of melatonin and discusses the findings in terms of

melatonin's actions on the neuroendocrine axis, the immune system, the gastrointestinal tract, and the pulmonary and cardiovascular systems in organisms ranging from unicellular animals to humans. Containing the most recent experimental data on the receptors which mediate the effects of the pineal hormone melatonin, this volume shows that melatonin receptors are more widely distributed than originally thought and exhibit wide species variations in terms of their distribution and density. In addition, multiple subtypes of melatonin receptors are identified. These findings indicate that melatonin is a ubiquitously-acting molecule which mediates a variety of physiologically important actions.