

The pineal complex of reptiles: physiological and behavioral roles

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The pineal complex of reptiles is a morphologically and functionally connected set of organs that originates as an evagination of the roof of the diencephalon. It is formed by two structures: the pineal organ and the parietal eye. The pineal gland is present in Chelonia, Squamata and Rhynchocephalia, but not in Crocodylia. The parietal eye is present in some species of lizards (Squamata) and in the tuatara (Rhynchocephalia). Both the pineal gland and the parietal eye are photosensitive. In particular, the parietal eye is an highly organized photoreceptive structure, with a well-defined lens, cornea and retina. The most important (and studied) secretory product of this complex is the hormone melatonin which is synthesized by both organs (pineal and parietal eye). The pineal organ is believed to be the neuroendocrine transducer of changes in photoperiod and environmental temperature and it has been demonstrated to have a functional role in many aspects of reptilian biology. Melatonin has an influence on the mechanisms controlling thermoregulation (behavioral and physiological), because its manipulation or removal may produce significant alterations of behavioral and physiological thermoregulatory parameters. The reptilian pineal complex may also possess self-sustained circadian oscillators which are involved in the circadian organization of these animals and in their reproduction. It is believed that many of the roles played by the pineal complex are mediated by the hormone melatonin, since exogenous administration of melatonin may affect the animal's physiology and/or behavior. The present paper will review the current knowledge about the neuroendocrinology and functional roles of the reptilian pineal complex.

KEY WORDS: parietal eye, pineal, melatonin, reptiles, thermoregulation, circadian rhythms, body temperature, locomotor activity.

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INTRODUCTION

The pineal complex of reptiles is a morphologically and functionally connected set of organs that originates as an evagination of the roof of the diencephalon. It is formed by two structures: the pineal organ and the parietal eye. The pineal organ (pineal gland or epiphysis cerebri) is present in Chelonia, Squamata and Rhynchocephalia, but not in Crocodylia, while the parietal eye (third eye or papapineal organ) is present in Rhynchocephalia and in some species of lizards (review in QUAY 1979).

The pineal gland of Chelonia, Sauria and Rhynchocephalia contains photosensory cells, however the ultrastructure and the number of these cells may vary among the species (HAMASAKI & EDER 1977, QUAY 1979, COLLIN & OKSCHE 1981, COLLIN et al. 1986). Usually, the photosensory cells have poorly organized outer segments and lack the regular stacked lamellar disks characteristic of rod or cone outer segments (QUAY 1979). A recent investigation in *Anolis carolinensis* has shown pineal cells that were labeled with rod and/or cone specific antibodies (FOSTER et al. 1993), but it is still unclear whether the antibody labeled different classes of pineal photoreceptors or a single opsin type with an epitope shared by rod-like and cone like opsins. The pineal gland of adult snakes does not contain photoreceptor-like cells, and the principal cell type is the pineal parenchymal cell. Most pineal innervation seems to be afferent, probably carries photic information, and projects to the pretectal and tegmental areas of the brain (HAMASAKI & EDER 1977, QUAY 1979). Efferent fibers have also been described, but the origin and function of these nerves is unknown (COLLIN et al. 1986).

The parietal eye has a well-defined lens, cornea and retina, with photoreceptor cells that morphologically resemble the cones of the lateral eyes (HAMASAKI & EDER 1977, QUAY 1979, ENGBRETSON 1992). Morphological analysis suggests that at least two types of photoreceptors may exist within the parietal eye. These photoreceptors synapse directly onto ganglion cells, the axons of which form the parietal nerve which subsequently innervates several areas of the brain, such as the habenular area, the dorsolateral nucleus of the thalamus, pretectal areas, the epihypothalamus, and probably also the pineal (KORF & WAGNER 1981, ISABEKOVA et al. 1987).

Several electrophysiological and biochemical investigations have confirmed the morphological evidence suggesting that the pineal gland and the parietal eye are both photoreceptive. However, although the pineal organ of reptiles does respond to light, it does not have a differential electrical response to chromatic light stimuli (DODT 1973). On the contrary, the parietal eye shows a chromatic response to visible light (review in ENGBRETSON 1992, but see also SOLESSIO & ENGBRETSON 1993) and there is also preliminary evidence for an ultraviolet-sensitive system (JENISON & NOLTE 1980). Other electrophysiological investigations have also demonstrated parietal eye unresponsiveness to infrared wavelengths, eliminating thermoreception as a functional role for the parietal eye (MILLER & WOLBARSH 1962; Fig. 1).

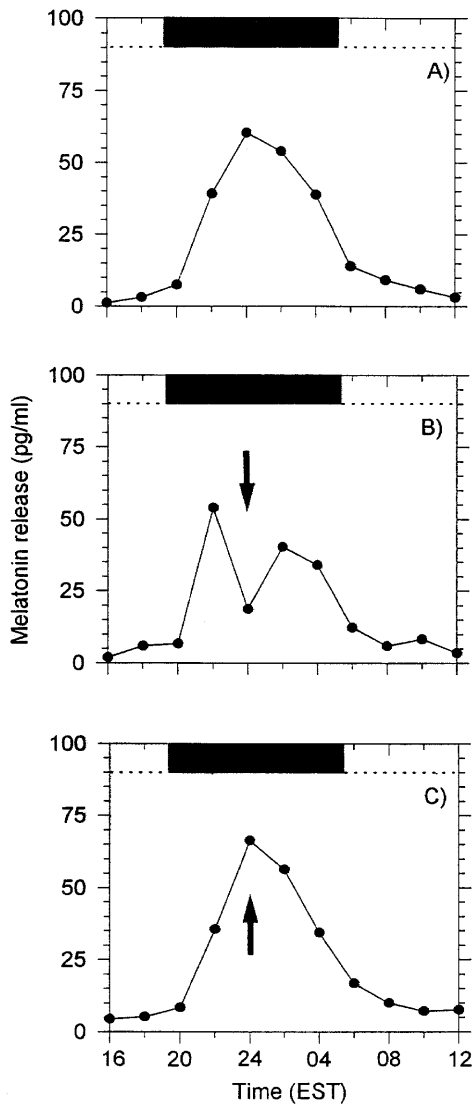


Fig. 1. — Melatonin release from cultured parietal eyes of *Anolis carolinensis* in L:D cycle (A) and when exposed in the middle of the night to 1 hr of white light (B) or 1 hr of red-infrared light (C). As shown by the graphs white light suppressed melatonin synthesis, whereas red-infrared light did not. Parietal eyes were individually cultured in a flow-through culture apparatus at the constant temperature of 27 °C while perfused with Medium 199 at the constant rate of 1 ml/hr. Sample were collected every 2 hr and melatonin content of the medium was measured by radioimmunoassay (periods of darkness are represented by the black bars at the

Interestingly, despite the strong electrophysiological evidence and the fact that the visual pigment(s) function in the parietal eye similarly to those of the retina (EAKIN 1973), FOSTER et al. (1993) failed to identify any opsin immunoreactive cells or any photopigment chromophore within the parietal eye.

NEUROENDOCRINOLOGY

The morphological aspects of the pineal photosensory cells gives clear evidence of their secretory activity (QUAY 1979, COLLIN & OKSCHE 1981). Melatonin is the key secretory product of the pineal complex and the steps in the manufacture of this hormone are well known (AXELROD 1974). Melatonin is synthesized from the amino acid tryptophan via a multi-enzymatic pathway. First, serotonin is synthesized from tryptophan by the enzymes tryptophan hydroxylase and aromatic amino acid decarboxylase. Serotonin is then converted to melatonin by the enzymes serotonin-*N*-acetyltransferase (SNAT) and hydroxyindole-*O*-methyltransferase (HIOMT). Although the details of melatonin metabolism have been studied most extensively in mammals (review in EBADI 1984), its metabolism in reptiles appears to be similar (GRACE & BESHARSE 1994). In almost all vertebrates melatonin is secreted by the pineal gland and the retina, however the gut, the testis, and the Harderian gland may also synthesize small amounts of melatonin. In reptiles melatonin is produced by the pineal, parietal eye, retina, and in the Harderian gland (Table 1), however it is believed that melatonin in the lateral eye

bottom of each plot). The arrows indicate the time at which light pulses were delivered. Further details about the methods used are reported in MENAKER & TOSINI (1996).

(and also in the parietal eye) plays a local role as a neuromodulator and/or regulator of photoreceptor metabolism and does not contribute to melatonin levels in the blood. In few particular cases, i.e., when pineal melatonin is absent or when melatonin is produced by the eyes in large amounts, it has been hypothesized that retinal melatonin plays a hormonal role by contributing to blood levels (ROTH et al. 1980, MENAKER 1985, MENDONCA et al. 1996a).

Because melatonin is not stored in the pineal but rapidly diffuses, blood levels of the hormone reflect pineal melatonin synthesis. Several investigations have examined the roles played by light and temperature in the control of melatonin levels

Table 1.

Reptilian tissues from which melatonin secretion, synthetic activity or content have been demonstrated.

| | Site(s) | Compound(s) | Reference(s) |
|-----------------------------------|----------------------------------------|-------------|----------------------------------------------------------------------------------------------------|
| Chelonia | | | |
| <i>Testudo hermanni</i> | Pineal, Blood | Melatonin | VIVIEN-ROELS et al. 1979; VIVIEN-ROELS & ARENDT 1979, 1981, 1983; VIVIEN-ROELS 1983, 1985 |
| <i>Chelonia mydas</i> | Blood | Melatonin | OWENS et al. 1980 |
| <i>Terrapene carolina</i> | Pineal, Blood | Melatonin | VIVIEN-ROELS et al. 1988, SKENE et al. 1989 |
| <i>Lissemys punctata</i> | Pineal | Serotonin | MAHAPATRA et al. 1986, 1988 |
| Rhynchocephalia | | | |
| <i>Sphenodon punctatus</i> | Blood | Melatonin | FIRTH et al. 1989a |
| Squamata | | | |
| <i>Dipsosaurus dorsalis</i> | Pineal, Blood, Retina | Melatonin | MENAKER 1985, JANIK & MENAKER 1990 |
| <i>Anolis carolinensis</i> | Pineal, Blood, Parietal eye, Retina | Melatonin | MENAKER & WISNER 1983, UNDERWOOD 1992, this paper |
| <i>Sceloporus occidentalis</i> | Pineal, Retina | Melatonin | MENAKER 1985 |
| <i>Iguana iguana</i> | Pineal, Blood, Parietal eye, Retina | Melatonin | TOSINI & MENAKER 1996, MENAKER & TOSINI 1996 |
| <i>Lampropholis guichenoti</i> | Pineal, Eye | HIOMT | JOSS 1978 |
| <i>Podarcis sicula</i> | Blood | Melatonin | FOÀ et al. 1992a |
| <i>Podarcis muralis</i> | Pineal | Serotonin | PETIT & VIVIEN-ROELS 1977 |
| <i>Trachydosaurus rugosus</i> | Pineal, Parietal eye | Melatonin | KENWAY et al. 1977; FIRTH et al. 1979, 1989a; FIRTH & KEN- WAY 1980, 1987 |
| <i>Christinus marmoratus</i> | Pineal | Melatonin | MOYER et al. 1995 |
| <i>Nerodia rhombifera</i> | Blood | Melatonin | TILDEN & HUTCHISON 1993 |
| <i>Thamnophis sirtalis</i> | Blood | Melatonin | MENDONCA et al. 1995, 1996a, 1996b |
| <i>Natrix tessellata</i> | Pineal, Retina, Harderian gland | Melatonin | VIVIEN-ROELS et al. 1981 |
| Crocodylia | | | |
| <i>Alligator mississippiensis</i> | Blood | Melatonin | ROTH et al. 1980 |

in many different species of reptiles. In natural conditions, the active tortoise *Testudo hermanni* showed high melatonin levels at night and low levels during the day. During their winter hibernation the levels were low and non-rhythmic (VIVIEN-ROELS et al. 1979, VIVIEN-ROELS & ARENDT 1981). Another laboratory study suggests that temperature is more important than light for the rhythmic expression of melatonin (VIVIEN-ROELS & ARENDT 1983). In the box turtle, *Terrapene carolina triunguis*, both light and temperature affect pineal and blood melatonin levels (VIVIEN-ROELS et al. 1988). In the water snake *Nerodia rhombifera* serum melatonin levels show a clear daily rhythm that is affected by photoperiod and temperature (TILDEN & HUTCHISON 1993). Seasonal changes in serum concentration of this hormone have been also demonstrated for the red garter snake, *Thamnophis sirtalis* (MENDONCA et al. 1995). In *Alligator mississippiensis*, which lacks a pineal organ, blood melatonin levels are low and arrhythmic (ROTH et al. 1980). In general, plasma melatonin levels show a daily variation, with higher levels during the dark phase. In the scincid lizard *Trachydosaurus rugosus* such a rhythm is present under rhythmic illumination (KENNAWAY et al. 1977; FIRTH et al. 1979; FIRTH & KENNAWAY 1980, 1987), but is absent in animals held in constant darkness (FIRTH et al. 1979). Also the tuatara (*Sphenodon punctatus*) shows a daily rhythm in melatonin levels (FIRTH et al. 1989a). In *Podarcis sicula* (FOÀ et al. 1992a), *Iguana iguana* (MENAHER & TOSINI 1996), and *Dipsosaurus dorsalis* (JANIK & MENAKER 1990) serum melatonin levels showed a daily rhythm which persisted when the animals were kept in constant darkness and temperature. In *T. rugosus* and *I. iguana* exposure of the animals to constant light produced low and arrhythmic levels of serum melatonin (FIRTH et al. 1979, TOSINI & MENAKER unpubl.). In reptiles, as in other vertebrates, it has been demonstrated that the pineal gland is the main, if not the only, source of blood-borne melatonin since pinealectomy abolishes circulating levels of melatonin (JANIK & MENAKER 1990, FOÀ et al. 1992a, TOSINI & MENAKER 1996).

The pineal of some fish, amphibians, reptiles (lizards), and birds contains circadian oscillators coupled with melatonin synthesis, whereas the mammalian pineal does not (review in MENAKER & TOSINI 1996). In the lizards *Anolis carolinensis*, *Sceloporus occidentalis*, *Dipsosaurus dorsalis*, *Iguana iguana*, and *Christinus marmoratus*, melatonin secretion from in vitro pineals can persist for many cycles (MENAHER & WISNER 1983, MENAKER 1985, JANIK & MENAKER 1990, MOYER et al. 1995, MENAKER & TOSINI 1996). Melatonin secretion in vitro has been shown to be always rhythmic in light:dark cycles; however, in constant conditions (i.e., in constant temperature and darkness) the pineal of *A. carolinensis*, *S. occidentalis* and *I. iguana* shows self-sustained rhythmicity (MENAHER & WISNER 1983, MENAKER 1985, MENAKER & TOSINI 1996), whereas the pineals of *D. dorsalis* and *C. marmoratus* it does not (JANIK & MENAKER 1990, MOYER et al. 1995). Exposure of the culture to constant light rendered the pineal organs arrhythmic, with only constant, low levels of melatonin secreted into the medium (MOYER et al. 1995; and Fig. 2). Rhythmic melatonin synthesis has also been demonstrated in the isolated pinealocytes of *A. carolinensis* (PICKARD & TANG 1993), and in the cultured parietal eyes of the lizards *I. iguana* and *A. carolinensis* (MENAHER & TOSINI 1996; Fig. 1).

Although melatonin is the major product of the pineal gland other compounds have been shown to be present in the pineal complex. Pineal serotonin levels show a daily rhythm in *T. hermanni* (VIVIEN-ROELS et al. 1979), *Lisemys punctata* (MAHAPATRA et al. 1986); and in *Podarcis muralis* (PETIT & VIVIEN-ROELS 1977; VIVIEN-ROELS 1983, 1985). Norepinephrine and epinephrine levels also show a daily variation in the pineal of *L. punctata* (MAHAPATRA et al. 1986, 1988).

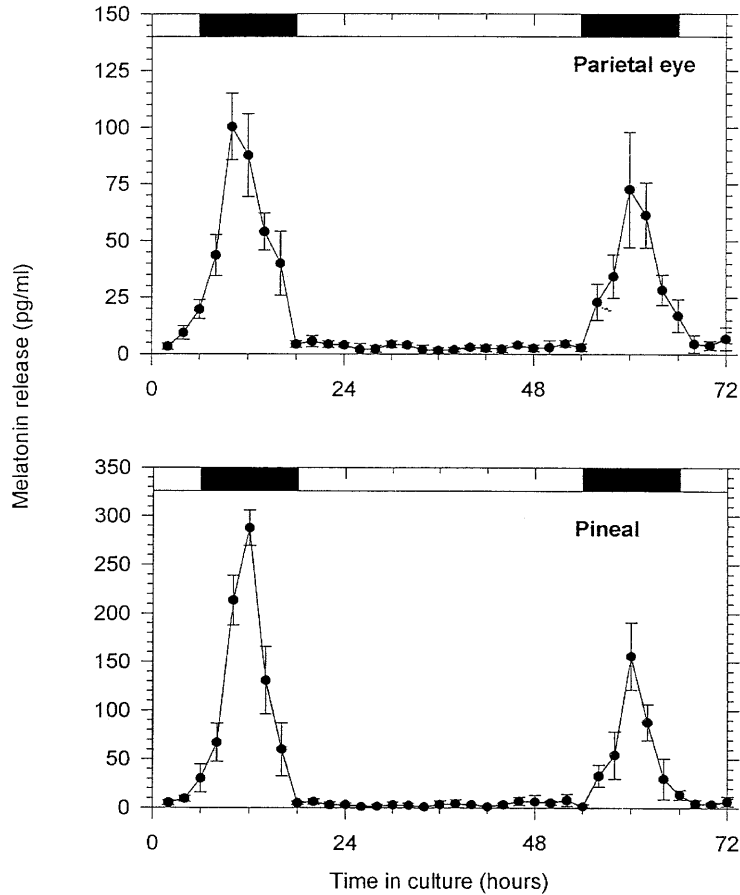


Fig. 2. — Mean melatonin release from cultured pineal glands ($n = 3$) of *Iguana iguana* exposed for 1 day in L:D cycle, 1 day in constant illumination, and again 1 day in L:D. Vertical bars represent standard error of the mean (SEM). Exposing the culture to constant light suppressed melatonin synthesis.

One of the most intriguing aspect of the pineal complex functioning is how the parietal eye and the pineal organ communicate and interact. Unfortunately, few investigations have addressed this issue. ENGBRETSON & LENT (1976), using an isolated parietal eye-pineal gland preparation, investigated how neurons in the pineal gland responded to changing levels of serotonin and norepinephrine and how that information is communicated to the parietal eye. In another study, BETHEA & WALKER (1978) demonstrated that HIOMT activity in the pineal was influenced by light impinging upon both the lateral and parietal eyes. However, this study also demonstrated that the greatest pineal response to light occurs through the lateral eyes. In a further study, TOSINI & AVERY (1996) suggested that the transient wavelength-dependent shift recorded after occlusion of the parietal eye (TOSINI & AVERY 1994)

may be compensated by the light information impinging on the lateral eyes. Such observations indicate that the role played by the parietal eye may be rather insignificant compared to that played by the lateral eye.

FUNCTIONAL ROLES

Thermoregulation

A great deal of information has accumulated relative to the role of melatonin in physiology; particularly in reference to reproduction and circadian rhythmicity. Several investigations have also shown that in vertebrates the pineal gland plays an important role in the control of thermoregulatory behavior and physiology as well as in the control of circadian and seasonal thermoregulation (review in HELDMAIER & LYNCH 1986, SAARELA & REITER 1994).

Reptiles depend on the external environment to provide the heat necessary for metabolism, because their metabolic heat production generally does not affect their body temperature. The regulation of body temperature in these animals is achieved by behavioral and/or physiological adjustments in relation to the thermal characteristics of the environment. The mechanism controlling thermoregulatory processes is not yet completely understood, but it is believed to be located in the hypothalamus (review in FIRTH & TURNER 1982). Many investigations suggest that the pineal complex and melatonin are involved in the control of thermoregulatory processes in reptiles (Table 2). Removal or shielding of the parietal eye, in both laboratory and in field conditions, resulted in an increased exposure to bright light and lengthened thermoregulatory basking (STEBBINS & EAKIN 1958, STEBBINS 1960, PACKARD & PACKARD 1972, STEBBINS & COHEN 1973). Parietalectomy, or shielding of the parietal eye, did not affect body temperature in *Sphenodon punctatus*, *Sceloporus occidentalis* (STEBBINS & EAKIN 1958, STEBBINS 1970) or in *Tropidurus albamarlensis* (STEBBINS & WILLHOFT 1966). On the other hand, parietalectomized lizards (*Leiocephalus carinatus*) maintained their body temperature at higher levels (PHILLIPS & HOWES 1988), while in *S. virgatus* a lower temperature was selected by the animals when buried (STEBBINS 1963). Other laboratory investigations have examined the effect of parietalectomy or parietal eye shielding on the daily rhythm of body temperature selection. In a thermal gradient, parietalectomized *A. carolinensis* selected higher temperature during the photophase (ROTH & RALPH 1976), or during both the photophase and scotophase (HUTCHISON & KOSH 1974). A similar result was obtained in *S. magister* (ENGBRETSON & HUTCHISON 1976). Shielding the parietal eye of *Lacerta viridis* reduced the temperature selected by this lizard during the dark phase of the light:dark cycle and during the light phase in summer, but not in spring or autumn (RISMILLER 1987). Shielding the parietal eye did not produce any change in the body temperature selection of *Crotaphytus collaris* when held in an environment with uniform illumination (FIRTH et al. 1989b, SIEVERT & HUTCHISON 1989). However, if specimens of *C. collaris* with shielded parietal eyes were kept in enclosures where only a small source of light was available, the preferred body temperature was higher and the daily cycle of temperature selection was abolished (SIEVERT & HUTCHISON 1989). Shielding the parietal did not alter the mean body temperature selected by *P. muralis* held in a thigmothermal gradient, however lizards with shielded parietal eye thermoregulate more precisely than sham shielded

Table 2.

Studies showing effects of parietectomy (PARX) or parietal eye shielding (PARC), Pinealectomy (PINX) and somministration exogenous melatonin (MEL) on the thermoregulation (Tb = body temperature; MST = mean selected temperature; TSP = thermoregulatory set points; UTSP = upper thermoregulatory set point).

| | Manipulation | Effect(s) | Reference(s) |
|--------------------------------|--------------|-----------------------|-----------------------------|
| Chelonia | | | |
| <i>Terrapene carolina</i> | MEL | decrease MBT | ERSKINE & HUTCHISON 1981 |
| Rhynchocephalia | | | |
| <i>Sphenodon punctatus</i> | PARX | no change | STEBBINS & EAKIN 1958 |
| Squamata | | | |
| <i>Sceloporus occidentalis</i> | PARX | no change | STEBBINS & EAKIN 1958 |
| <i>Sceloporus occidentalis</i> | PARC | higher Tb | STEBBINS & EAKIN 1958 |
| <i>Sceloporus occidentalis</i> | PINX | lower Tb | STEBBINS 1960 |
| <i>Sceloporus virgatus</i> | PARX | lower Tb | STEBBINS 1960 |
| <i>Sceloporus virgatus</i> | PARC | lower Tb when buried | STEBBINS 1963 |
| <i>Sceloporus magister</i> | PARX | higher Tb | ENGBRETSON & HUTCHISON 1976 |
| <i>Tropidurus albamarensis</i> | PARX | no effect | STEBBINS & WILLHOFT 1966 |
| <i>Anolis carolinensis</i> | PARX | higher Tb | HUTCHISON & KOSH 1974 |
| <i>Anolis carolinensis</i> | PARX | higher Tb in the day | ROTH & RALPH 1976 |
| <i>Phrynosoma douglassi</i> | PARC | higher TSP | PHILLIPS et al. 1980 |
| <i>Phrynosoma douglassi</i> | PARC | higher UTSP | PHILLIPS & HARLOW 1981 |
| <i>Leiocephalus carinatus</i> | PARC | higher Tb | PHILLIPS & HOWES 1988 |
| <i>Crotaphytus collaris</i> | PARX | higher Tb | FIRTH et al. 1988 |
| <i>Crotaphytus collaris</i> | PINX | lower MST | FIRTH et al. 1980, 1989b |
| <i>Crotaphytus collaris</i> | PARC | no effect | FIRTH et al. 1989b |
| <i>Crotaphytus collaris</i> | PARC | higher Tb | SIEVERT & HUTCHISON 1989 |
| <i>Crotaphytus collaris</i> | MEL | higher Tb (day) | COTHRAN & HUTCHISON 1979 |
| <i>Sauromalus obesus</i> | PINX | no effect | FIRTH et al. 1989b |
| <i>Iguana iguana</i> | PARX | higher MST | TOSINI & MENAKER 1996 |
| <i>Iguana iguana</i> | PINX | lower MST (day) | TOSINI & MENAKER 1996 |
| <i>Iguana iguana</i> | MEL | higher MST (day) | TOSINI & MENAKER 1996 |
| <i>Cordylus vittifer</i> | MEL | lower MST | SKINNER 1991 |
| <i>Lacerta viridis</i> | PARC | lower Tb | RISMILLER 1987 |
| <i>Lacerta viridis</i> | MEL | lower MST | RISMILLER & HELDMAIER 1987 |
| <i>Lacerta vivipara</i> | PARC | lower TSP | JONES 1989 |
| <i>Podarcis sicula</i> | PARC | no effect | This paper |
| <i>Podarcis sicula</i> | PINX | higher TSP | TOSINI et al. 1996 |
| <i>Podarcis muralis</i> | PARC | lower TSP (transient) | TOSINI & AVERY 1994 |
| <i>Podarcis muralis</i> | PARC | no effect on MST | McKEEHAN & SIEVERT 1996 |

lizards during part of the day (McKEEHAN & SIEVERT 1996). In *P. sicula* parietectomy temporarily abolished the circadian rhythm of body temperature selection (INNOCENTI et al. 1993). In *I. iguana* parietectomy produced only a transient increase in body temperature selection during the first or second night following the operation (TOSINI & MENAKER 1996).

Other studies have investigated the effects that impairment of the parietal eye produces on the thermoregulatory set points controlling the thermoregulatory behavior. Shielding the parietal eye of *P. douglassi* produced a significant increase in both

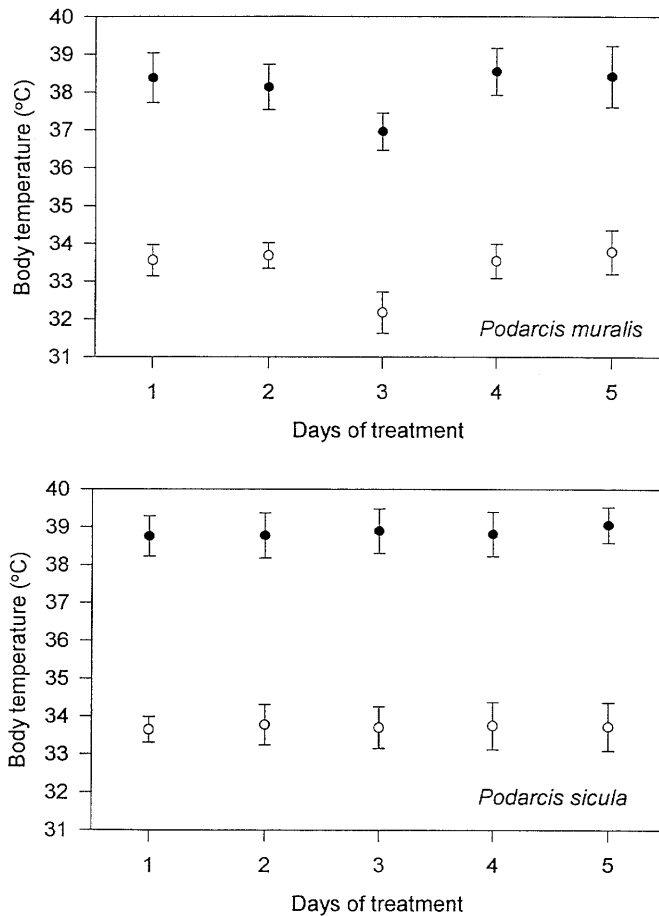


Fig. 3. — Overall mean values (\pm SD) of upper (black circles) and lower (white circles) thermoregulatory set point temperatures during 5 days in which the parietal eye was covered by a layer of black paint. A transient decrease in upper and lower thermoregulatory set points was recorded in *P. muralis*, but not in *P. sicula* (Multiple Comparison and Friedman tests, $P < 0.05$ and > 0.1 respectively). Thermoregulatory set point temperatures were measured in freely moving animals by thermography as described in TOSINI & AVERY (1993).

thermoregulatory set points (PHILLIPS et al. 1980) or just in the upper set point (PHILLIPS & HARLOW 1981). In *P. muralis* (TOSINI 1993) and in *Lacerta vivipara* (JONES 1989) occlusion of the parietal eye decreased both thermoregulatory set points, while no effect was recorded in *P. sicula* (see Fig. 3). In *P. muralis* the decrease of the set points was transient and wavelength-dependent (TOSINI & AVERY 1994).

Interestingly, a geographical trend has been observed in lizard species possessing the parietal eyes (GUNDY et al. 1975). In lizard families of widespread distribution species living in lower latitudes generally lack a parietal eye, whereas those species inhabiting mid and high latitudes possess one. Since thermoregulatory

costs are greater in temperate zone than in tropical or semi-tropical ones, the occurrence of the parietal eye in species inhabiting temperate areas reinforces the hypothesis that this organ is involved in thermoregulation.

Considerably less attention has been directed to the possible thermoregulatory role of the pineal gland. STEBBINS (1960) found through field studies that pinealectomized *S. occidentalis* had lower mean temperatures than control animals. More recently it has been shown that pinealectomized *C. collaris* behaviorally select lower temperatures in laboratory thermal gradients (FIRTH et al. 1980, 1989b) and in outdoor enclosures (FIRTH et al. 1988). Pinealectomy in *Sauromalus obesus*, on the other hand, did not have any effect on the thermal preference of the animals (FIRTH et al. 1989b). In *P. sicula*, pinealectomy abolished the rhythm of temperature selection in the 2-3 weeks following the operation (INNOCENTI et al. 1993) and increased the thermoregulatory set point temperatures (TOSINI et al. 1996). Pinealectomized *I. iguana* maintain their body temperature at significantly lower levels during the day and at significantly higher levels during the night than did sham-operated or control animals (TOSINI & MENAKER 1996).

It is important to note that in all the investigations mentioned above pinealectomized animals were also without their parietal eye, because removal of the pineal gland without damaging the parietal eye it is difficult or impossible in any case.

Since it has been convincingly shown that the pineal complex influences behavioral thermoregulation, it could be hypothesized that physiological thermoregulation may also be affected by manipulation of the pineal complex. Panting threshold is one of the few physiological measures of thermoregulation that has been conclusively shown to be affected by manipulation of the pineal complex. As early as 1902 a series of experiments on the North African lizards *Uromastix acanthinurus* and *Varanus arenarius* found that the panting response to high temperatures depends upon light falling directly upon the parietal eye, with the response inhibited by interposing an opaque screen (LANGLOIS 1902). Many years later another investigation in the lizard *Amphibolurus muricatus* showed that parietectomy elicited a seasonally dependent depression of panting threshold and abolished the diel variation in panting (FIRTH & HEATWOLE 1976). Oxygen consumption may also be affected by manipulation of the pineal complex. In *Sceloporus cynogenys* removal of the parietal eye had no effect on the maximum levels of oxygen consumption, while lateral eye removal will elevate the maximal level. Yet removal of both the parietal eye and the lateral eyes returns oxygen consumption back to its normal level (SONGDAHL & HUTCHISON 1972), suggesting that the parietal and the lateral eyes interact in some way to determine the rates of metabolism. Parietalectomy did not affect the oxygen consumption of *S. occidentalis* (FRANCIS & BROOKS 1970). Parietalectomized *A. carolinensis* showed a lower critical thermal maximum (KOSH & HUTCHISON 1972) while in *S. occidentalis* FRANCIS & BROOKS (1970) reported that parietectomy did not alter heart and ventilatory rate, both indicators of oxygen consumption. In *C. collaris* parietectomy did not affect heart rate, while pinealectomy caused an elevation of heart rate at higher head temperature (RALPH et al. 1979). A recent investigation in *I. iguana* has demonstrated the presence of an endogenously generated circadian rhythm of body temperature when the animals are kept at a constant temperature (TOSINI & MENAKER 1995); this rhythm is not affected by parietectomy, whereas pinealectomy abolishes the rhythm (MENAKER & TOSINI 1996).

The observation that manipulation of the pineal complex affects thermoregulatory processes, taken together with the fact that melatonin is mostly produced in the pineal complex (see previous section), suggests that some of the thermoregula-

tory changes observed may be mediated by melatonin. Indeed, some studies have demonstrated that administration of exogenous melatonin may produce a significant alteration of thermoregulatory mechanisms. Injections of melatonin in the turtle *Terrapene carolina* significantly decreased the mean selected temperature (ERSKINE & HUTCHISON 1981). In lizards melatonin injections lowered mean selected temperature in *Cordylus vittifer* (SKINNER 1991), and in *C. collaris* lower mean temperatures were recorded during the scotophase and higher temperatures during the photophase (COTHRAN & HUTCHISON 1979). In *L. viridis* melatonin implants decreased the mean selected temperatures during the night (RISMILLER & HELDMAIER 1987). In pinealectomized *I. iguana* melatonin injections decreased the body temperature selected by the lizard during the night and increased the body temperatures selected during day (TOSINI & MENAKER 1996). In *A. muricatus* injections of melatonin lowered the panting threshold and abolished its daily variation (FIRTH & HEATWOLE 1976).

Activity rhythms and circadian organization

It is well known that most organisms can exhibit daily rhythms of a wide number of behavioral, physiological, and biochemical parameters. Even when the organism is maintained under constant light and temperature conditions, most of these daily rhythms will persist, thus demonstrating that they are driven by endogenous oscillators. Rhythms that persist in constant conditions with a periodicity close to 24 hr are called circadian. The pineal gland has been shown to be a central component in the regulation of circadian rhythms in reptiles (Table 3) and in other non-mammalian vertebrates (review in UNDERWOOD 1990). In some species of cyclostomes, fishes, and amphibians the circadian rhythm of locomotor activity is abolished by pinealectomy (review in UNDERWOOD 1990; but see also MENAKER & TOSINI 1996). Pinealectomy abolishes circadian body temperature and locomotor activity rhythms in the house sparrow and abolishes the rhythm of locomotor activity in several other species birds. The role that the pineal gland plays in the circadian organization of mammals is more obscure, since pinealectomy, thereby abolishing the rhythm of circulating melatonin, has little or no effect on observed physiological functions (review in CASSONE 1990). In reptiles the pineal complex plays a role in both circadian photoreception (i.e., to entrain endogenous rhythms with exogenous cycles) and pacemaker activity (i.e., the rhythmic control of physiology and behavior).

Circadian photoreception. The anatomical and functional organization of the parietal eye and of the pineal organ (see Neuroendocrinology section) indicates that these photoreceptive structures are not capable of forming images, suggesting an involvement of these organs in other sensory tasks. Indeed, several observations of the effects of light:dark cycles on the circadian activity rhythms of blinded lizards show that, in reptiles, light is sensed by extra-retinal photoreceptors and that these photoreceptors can mediate circadian entrainment. Removal of the lateral eyes do not prevent the entrainment of *A. carolinensis*, *S. olivaceus*, *S. magister*, *S. occidentalis*, *S. clarki*, *Xantusia vigilis*, *Hemidactylus turcicus*, *Coleonyx variegatus*, *I. iguana* and *P. sicula* (UNDERWOOD & MENAKER 1970, 1976; UNDERWOOD 1973, 1985a; FOA et al. 1993; TOSINI & MENAKER unpubl.). However, removal of the pineal gland of *C.*

Table 3.

Studies showing effects of parietectomy (PARX), pineaectomy (PINX) and administration exogenous melatonin (MEL) on circadian rhythms (CRL = circadian rhythm of locomotor activity; CRT = circadian rhythm of body temperature; BTS = circadian rhythm of behavioral temperature selection; τ = free-running periods).

| | Manipulation | Effect(s) | Reference(s) |
|--------------------------------|--------------|--------------------------------------------------------------------|---------------------------------------|
| <i>Anolis carolinensis</i> | PARX | no change in CRL | UNDERWOOD 1983 |
| <i>Anolis carolinensis</i> | PINX | arrhythmicity in CRL | UNDERWOOD 1981, 1983 |
| <i>Sceloporus olivaceus</i> | PINX | changed τ and a of CRL | UNDERWOOD 1977 |
| <i>Sceloporus olivaceus</i> | MEL | increased τ of CRL | UNDERWOOD 1979 |
| <i>Sceloporus olivaceus</i> | MEL | arrhythmicity in LL of CRL | UNDERWOOD 1979 |
| <i>Sceloporus occidentalis</i> | PINX | increased τ of CRL | UNDERWOOD 1981 |
| <i>Sceloporus occidentalis</i> | MEL | increased τ of CRL | UNDERWOOD 1979, 1981 |
| <i>Sceloporus occidentalis</i> | MEL | entrained CRL in intact animals | UNDERWOOD & HARLESS 1985 |
| <i>Sceloporus occidentalis</i> | MEL | entrained CRL in PINX, animals | HYDE & UNDERWOOD 1995 |
| <i>Dipsosaurus dorsalis</i> | PINX | no effect on CRL | JANIK & MENAKER 1990 |
| <i>Dipsosaurus dorsalis</i> | MEL | increased in τ of CRL | JANIK & MENAKER 1990 |
| <i>Iguana iguana</i> | PARX | no effect on CRL but CRA was less robust and change in τ | MENAKER & TOSINI 1996 |
| <i>Iguana iguana</i> | PINX | change in τ of CRL, and CRT was abolished | MENAKER & TOSINI 1996 |
| <i>Gallotia galloti</i> | PINX | arrhythmicity of CRL | MOLINA-BORJA 1996 |
| <i>Podarcis sicula</i> | PINX | change in τ of CRL with the effects changing with the seasons | FOÀ 1991; INNOCENTI et al. 1993, 1996 |
| <i>Podarcis sicula</i> | PARX | no effect on CRL | INNOCENTI et al. 1993 |
| <i>Podarcis sicula</i> | MEL | increased τ | FOÀ et al. 1992b |
| <i>Podarcis sicula</i> | PARX | BTS was temporarily abolished (1 week) | INNOCENTI et al. 1993 |
| <i>Podarcis sicula</i> | PINX | BTS was temporarily abolished (2-3 weeks) | INNOCENTI et al. 1993 |

variegatus or removal of both the pineal gland and the parietal eye of *S. olivaceus*, *S. magister* (UNDERWOOD 1973) or *P. sicula* (FOÀ et al. 1993) does not prevent entrainment to light:dark cycles in animals with lateral eyes removed. Such observations demonstrate the presence of another class of extra-retinal photoreceptors capable of mediating entrainment of circadian rhythms and shows that the parietal eye and/or the pineal gland are not necessary for the entrainment of circadian rhythms of locomotor activity (UNDERWOOD & MENAKER 1976). Such extra-retinal photoreceptors are thought to be located in the deep brain and, in the lizards *A. carolinensis* and *I. iguana*, they have been putatively identified in the basal region of the lateral ventricles (FOSTER et al. 1994, GRACE et al. 1996).

Pacemaker activity. It has been shown that the pineal of some lizard contains self-sustained circadian oscillators (MENAKER & WISNER 1983, MENAKER & TOSINI 1996) and the removal of the pineal complex effects the expression of circadian

rhythmicity. Pinealectomy abolished circadian rhythms of locomotor activity in *A. carolinensis* (UNDERWOOD 1983), *Gallotia galloti* (MOLINA-BORJA 1996), and produced marked changes in the freerunning periods of *S. olivaceus*, *S. occidentalis* (UNDERWOOD 1981, 1983) and *P. sicula* (FOÀ 1991, INNOCENTI et al. 1996). In *D. dorsalis* pinealectomy has no effects on circadian locomotor activity rhythms (JANIK & MENAKER 1990). In *P. sicula* the effects of pinealectomy on the locomotor activity rhythm are seasonally dependent (INNOCENTI et al. 1996) and pinealectomy temporarily abolishes the rhythm of body temperature selection (INNOCENTI et al. 1993). In *I. iguana* pinealectomy abolishes the circadian rhythm of body temperature, but has no effect on the circadian rhythm of locomotor activity (MENAKER & TOSINI 1996). The involvement of the lizard's parietal eye in the control of daily activity and circadian organization is more obscure. Experiments with *Anguis fragilis* suggest that this structure may affect the animal's activity rhythm; parietalectomized animals tended to desynchronize from the light cycle and showed considerably more activity than intact animals. Furthermore, exposing animals with their parietal eye removed to green light resulted in an increase in their overall activity, while held under violet light the activity of these animals were reduced (PALENSCHAT 1964). GLASER (1958) found an increase in activity upon shielding the parietal eye of desert night lizards (*Xantusia vigilis*). Parietalectomized lizards of the same species, when kept in a constant thermal environment, selected the more brightly illuminated region of the gradient (STEBBINS 1960). In the species so far studied, removal of the parietal eye does not affect the circadian rhythms of locomotor activity (review in UNDERWOOD 1992). However, recent studies have shown an involvement of the parietal eye in the expression of the circadian rhythm of body temperature (MENAKER & TOSINI 1996) and in the circadian rhythm of body temperature selection (INNOCENTI et al. 1993).

Chronic administration of exogenous melatonin lengthened the period of the freerunning activity rhythm in two iguanid lizard species (*S. occidentalis* and *S. olivaceus*) and induced arrhythmicity in *S. olivaceus* when held in constant light (UNDERWOOD 1979). Lengthening of the freerunning period was also recorded in *D. dorsalis* (JANIK & MENAKER 1990) and *P. sicula* (FOÀ et al. 1992b). Daily infusions of melatonin entrained the locomotor activity rhythms in both pinealectomized and intact *S. occidentalis* (HYDE & UNDERWOOD 1995).

These observations provide strong support for the hypothesis that the pineal, via its circadian rhythm of melatonin secretion, plays an important role in the circadian organization of reptiles. However, these studies also suggest that there are inter-specific differences in the role that the pineal gland plays in the circadian system of these vertebrates, and that pineal influence may vary with the season (INNOCENTI et al. 1996). These results also suggest that the pineal acts as a pacemaker within a multioscillatory circadian system and that the inter- and intraspecific differences recorded in response to pinealectomy can be explained by variations in the strength of coupling among the different circadian oscillators.

Reproductive physiology

In comparison to the extensive work on pineal-gonadal relations in mammals and birds (review in TUREK & VAN CAUTER 1994) there are fewer experiments testing such a physiological relationship in reptiles. However, the data available sug-

gests that the parietal eye and the pineal gland may be involved in the control of gonadal physiology (CLAUSEN & PORIS 1937, LICHT & PEARSON 1970, UNDERWOOD 1985b). In *A. carolinensis* parietectomy in late spring (March-June) had inhibitory effects on the testes. When parietectomy was performed in the winter (December-March) no effect was recorded. However, parietectomy plus blinding was more effective than either procedure alone (RIDGEWAY & KENT 1971). Pinealectomy, and subsequent evaluation of its effects on the ovaries, has provided clearer evidence of the relationship between the pineal and the gonads (LEVEY 1973). Pinealectomy in winter elicited a significant follicular development within 2 weeks; effects that were reversed by daily injections of melatonin (LEVEY 1973). More recent studies have confirmed that the pineal gland and melatonin may affect gonadal condition in the lizards *Calotes versicolor* (HALDAR & THAPLIYAL 1977, 1981; MISRA & THAPLIYAL 1979), *A. carolinensis* (UNDERWOOD 1985b) and in the snake *Natrix piscator* (HALDAR & PANDEY 1989a, 1989b). The effects recorded, just as in other vertebrates, can be either pro- or anti-gonadal, depending on the time of year in which surgery is done, or exogenous melatonin is given. Hence, via melatonin the pineal gland may "per se" affects reproductive behavior: for example, if gonads fail to recrudescence because of high melatonin levels, sex steroid levels remain low, and mating behavior is not activated. Very few studies have investigated pineal and melatonin involvement in the expression of sexual behavior. Pinealectomy in the fall inhibits courtship behavior in the majority of male garter snakes (*T. sirtalis parietalis*) the following spring (NELSON et al. 1987, CREWS et al. 1988, MENDONCA et al. 1996a). A further investigation showed that pinealectomized *T. sirtalis* had detectable levels of melatonin, pinealectomized males showing courtship behavior retained a daily melatonin rhythm. On the contrary, pinealectomized animals with disrupted cycles did not show courtship behavior (MENDONCA et al. 1996b). However, in male garter snakes melatonin implants failed to modulate courtship behavior in both pinealectomized and sham operated animals (MENDONCA et al. 1996a).

Other roles

Other investigations on the function of pineal complex either have not been carried to meaningful depth or have provided fragmentary result that often are difficult, if not impossible, to interpret. Among these findings are those concerning color changes in *A. carolinensis* following either the removal or covering of the parietal eye (MEYER & BROOKS 1968), increased aggressiveness in *L. carinatus* (PHILLIPS & HOWES 1988), and energy expenditure in some lizards (BICKLER & NAGY 1980). A role for the parietal eye has also been demonstrated for homing behavior (BISSINGER 1980). ELLIS-QUINN & SIMON (1991) showed that in *Sceloporus jarrovi* parietal eye manipulation (parietectomy or painting the parietal eye) affected homing behavior, and the authors suggested that the parietal eye is critical for the perception of the celestial cues utilized in orientation. They hypothesized that the parietal eye acts as a specialized analyzer of the e-vector of linearly polarized light, given that since the parietal eye photoreceptors are arranged in a pattern that may allow for the analysis of polarized light (HAMASAKI & EDER 1977). This interesting hypothesis is supported by the fact that shielding the parietal eye of the lizard *Uma notata* prevents trained animals from orienting polarotactically (ADLER & PHILLIPS 1985).

CONCLUSIONS

The data gathered so far indicate that the pineal complex shows a wide degree of variability within the class Reptilia. Such variability is present at the level of structure (i.e., the presence or absence of the parietal eye, presence or absence of the pineal, and the presence or absence of photoreceptive cells within the pineal), and at neuro-endocrinological level (i.e., the presence or absence of a circadian oscillators coupled with melatonin synthesis within the pineal).

The pineal complex is certainly involved in the control of thermoregulatory processes; time lags between the removal and the manifestation of the effects suggest that these effects are hormonally mediated, probably via melatonin. It must be also noticed that the role of the pineal complex may vary among systematic groups within the class since in iguanid lizards, pineal complex manipulation produces opposite effects to those observed in lacertid lizards. Such variability is also present at the level of pineal involvement in the circadian organization since its removal may elicit arrhythmicity, changes in the length of the free-running period, or no effect.

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REFERENCES

- ADLER K. & PHILLIPS J.B. 1985. Orientation in a desert lizard (*Uma notata*): time-compensated compass movement and polarotaxis. *Journal of Comparative Physiology* 156: 547-552.
- AXELROD J. 1974. The pineal gland: a neurochemical transducer. *Science* 184: 134-148.
- BETHEA C.L. & WALKER R.F. 1978. Parietal eye-pineal gland interactions in the lizard *Sceloporus occidentalis* (Reptilia, Lacertilia, Iguanidae). *Journal of Herpetology* 12: 83-87.
- BICKLER P.E. & NAGY K.A. 1980. Effects of parietectomy on energy expenditure in free ranging lizards. *Copeia*: 923-925.
- BISSINGER B.E. 1980. Role of the parietal eye in the homing behavior of a lizard. *American Zoologist* 20: 842.
- CASSONE M.V. 1990. Effects of melatonin on vertebrate circadian systems. *Trends in Neurosciences* 13: 457-464.
- CLAUSEN H.J. & PORIS E.G. 1937. The effect of light upon sexual activity in the lizard, *Anolis carolinensis*, with special reference to the pineal body. *Anatomical Records* 69: 39-53.
- COLLIN J.P., FALCON J., VOISIN P. & BRISSON P. 1986. The pineal organ: ontogenetic differentiation of photoreceptor cells and pinealocytes, pp. 14-30. In: Gupta D. & Reiter R.J., Edits. The pineal gland during development from fetus to adult. London: Croom Helm.
- COLLIN J.P. & OKSCHE A. 1981. Structural and functional relationships in the nonmammalian pineal gland, pp. 27-67. In: Reiter R.J., Edit. The pineal gland: anatomy and biochemistry. Boca Raton, FL: CRC Press.
- COTHRAN M.L. & HUTCHISON V.H. 1979. Effect of melatonin on thermal selection by *Crotaphytus collaris* (Squamata, Iguanidae). *Comparative Biochemistry and Physiology* 63A: 461-466.
- CREWS D., HINGORANI V. & NELSON R.J. 1988. Role of the pineal gland in the control of annual reproductive behavioral and physiological cycles in the red-sided garter snake (*Thamnophis sirtalis parietalis*). *Journal of Biological Rhythms* 3: 293-302.

- DODT E. 1973. The parietal eye (pineal and parietal organs) of lower vertebrates, pp. 113-140. In: Jung R., Edit. *Handbook of sensory physiology. Heidelberg: Springer Verlag.*
- EAKIN R.M. 1973. The third eye. *Berkeley: University of California Press.*
- EBADI M. 1984. Regulation of the synthesis of melatonin and its significance to neuroendocrinology, pp. 1-38. In Reiter R.J., Edit. *The pineal gland. New York: Raven Press.*
- ELLIS-QUINN B.A. & SIMON C.A. 1991. Lizard homing behavior: the role of the parietal eye during displacement and radio-tracking, and time-compensated celestial orientation in the lizard *Sceloporus jarrovi*. *Behavioral Ecology and Sociobiology* 28: 397-407.
- ENGBRETSON G.A. 1992. Neurobiology of the lacertilian parietal eye system. *Ethology Ecology & Evolution* 4: 89-107.
- ENGBRETSON G.A. & HUTCHISON V.H. 1976. Parietal eye-pineal gland interactions in the lizard *Sceloporus occidentalis*. *Journal of Herpetology* 12: 83-87.
- ENGBRETSON G.A. & LENT C.M. 1976. Parietal eye of the lizard: neural photoresponses and feedback from the pineal gland. *Proceedings of the National Academy of Sciences, U.S.A.* 73: 654-657.
- ERSKINE D.J. & HUTCHISON V.H. 1981. Melatonin and behavioral thermoregulation in the turtle, *Terrapene carolina triunguis*. *Physiology and Behavior* 26: 991-995.
- FIRTH B.T. & HEATWOLE H. 1976. Panting thresholds of lizards: the role of the pineal complex in panting responses in an agamid, *Amphibolurus muricatus*. *General and Comparative Endocrinology* 29: 388-401.
- FIRTH B.T. & KENNAWAY D.J. 1980. Plasma melatonin levels in the scincid lizard *Trachydosaurus rugosus*. The effects of parietal eye and lateral eye impairment. *Journal of Experimental Biology* 85: 311-321.
- FIRTH B.T. & KENNAWAY D.J. 1987. Melatonin content of pineal, parietal eye and blood plasma of the lizard, *Trachydosaurus rugosus*: effect of constant and fluctuating temperature. *Brain Research* 404: 313-318.
- FIRTH B.T., KENNAWAY D.J. & ROZENBILDS M.A.M. 1979. Plasma melatonin in the scincid lizard, *Trachydosaurus rugosus*: diel rhythm, seasonality, and the effect of constant light and constant darkness. *General and Comparative Endocrinology* 37: 493-500.
- FIRTH B.T., MAULDIN R.E. & RALPH C.L. 1988. The role of the pineal complex in behavioural thermoregulation in the collared lizard *Crotaphytus collaris* under seminatural conditions. *Physiological Zoology* 61: 176-185.
- FIRTH B.T., RALPH C.L. & BOARDMAN T.J. 1980. Independent effects of the pineal and a bacterial pyrogen in behavioural thermoregulation in lizards. *Nature* 285: 399-400.
- FIRTH B.T., THOMPSON M.B. & KENNAWAY D.J. 1989a. Thermal sensitivity of reptilian melatonin rhythms: "cold" tuatara vs. "warm" skink. *American Journal of Physiology* 256: R1160-R1163.
- FIRTH B.T. & TURNER J.S. 1982. Sensory, neural and hormonal aspects of thermoregulation, pp. 213-274. In: Gans C. & Pough F.H., Edits. *Biology of the Reptilia* 12, *Physiology C, Physiological Ecology. London: Academic Press.*
- FIRTH B.T., TURNER J.S. & RALPH C.L. 1989b. Thermoregulatory behaviour in two species of iguanid lizards (*Crotaphytus collaris* and *Sauromalus obesus*): diel variation and the effect of pinealectomy. *Journal of Comparative Physiology (B)* 159: 13-20.
- FOÀ A. 1991. The role of pineal and the retinae in the expression of circadian locomotor rhythmicity in the ruin lizard, *Podarcis sicula*. *Journal of Comparative Physiology (A)* 169: 201-207.
- FOÀ A., FLAMINI M., INNOCENTI A., MINUTINI L. & MONTEFORTI G. 1993. The role of extraretinal photoreception in the circadian system of the ruin lizard *Podarcis muralis*. *Comparative Biochemistry and Physiology* 105A: 223-230.
- FOÀ A., JANIK D. & MINUTINI L. 1992a. Circadian rhythms of plasma melatonin in the ruin lizard *Podarcis sicula*: effects of pinealectomy. *Journal of Pineal Research* 12: 109-113.
- FOÀ A., MINUTINI L. & INNOCENTI A. 1992b. Melatonin a coupling device between oscillators in the circadian system of the ruin lizard, *Podarcis sicula*. *Comparative Biochemistry and Physiology* 103A: 719-723.
- FOSTER R.G., GARCIA-FERNANDEZ J.M., PROVENCIO I. & DEGRIP W. 1993. Opsin localization and

- chromophore retinoids identified within the basal brain of the lizard *Anolis carolinensis*. *Journal of Comparative Physiology (A)* 172: 33-45.
- FOSTER R.G., GRACE M.S., PROVENCIO I., DEGRIP W.J. & GARCIA-FERNANDEZ J.M. 1994. Identification of vertebrate deep brain photoreceptors. *Neuroscience and Biobehavioral Reviews* 18: 541-546.
- FRANCIS C. & BROOKS G.R. 1970. Oxygen consumption, rate of heart beat and ventilatory rate in parietectomized lizards, *Sceloporus occidentalis*. *Comparative Biochemistry and Physiology* 35: 463-469.
- GLASER R. 1958. Increase in locomotor activity following shielding of the parietal eye in night lizards. *Science* 128: 1577-1578.
- GRACE M.S., ALONES V., MENAKER M. & FOSTER R.G. 1996. Light perception in the vertebrate brain: an ultrastructural analysis of opsin- and vasoactive intestinal polypeptide immunoreactive neurons in iguanid lizards. *Journal of Comparative Neurology* 367: 575-594.
- GRACE M.S. & BESHARSE J.C. 1994. Melatonin deacetylase activity in the pineal glands and brains of the lizards *Sceloporus jarrovi* and *Anolis carolinensis*. *Neuroscience* 62: 615-623.
- GUNDY G.C., RALPH C.L. & WURST G.Z. 1975. Parietal eyes in lizards: zoogeographical correlates. *Science* 190: 671-673.
- HALDAR C. & PANDEY R. 1989a. Effect of pinealectomy on annual testicular cycle of Indian checkered snake, *Natrix piscador*. *General and Comparative Endocrinology* 76: 214-222.
- HALDAR C. & PANDEY R. 1989b. Effect of pinealectomy on the testicular response of the freshwater snake, *Natrix piscador*, to different environmental factors. *Canadian Journal of Zoology* 67: 2352-2357.
- HALDAR C. & THAPLIYAL J.P. 1977. Effect of pinealectomy on the annual testicular cycle of *Calotes versicolor*. *General and Comparative Endocrinology* 32: 395-399.
- HALDAR C. & THAPLIYAL J.P. 1981. Chronohaematological changes in the lizard *Calotes versicolor* after pinealectomy. *Annales d'Endocrinologie, Paris* 42: 35-41.
- HAMASAKI D.I. & EDER D.J. 1977. Adaptive radiation of the pineal system, pp. 497-548. In: Crescitelli F., Edit. Handbook of sensory physiology. *New York: Springer-Verlag*.
- HELDMAIER G. & LYNCH G.R. 1986. Pineal involvement in thermoregulation and acclimatization. *Pineal Research Review* 4: 97-139.
- HUTCHISON V.H. & KOSH R.J. 1974. Thermoregulatory function of the parietal eye in the lizard *Anolis carolinensis*. *Oecologia* 16: 173-177.
- HYDE L.L. & UNDERWOOD H. 1995. Daily melatonin infusions entrain the locomotor activity of pinealectomized lizards. *Physiology and Behavior* 58: 943-951.
- INNOCENTI A., BERTOLUCCI C., MINUTINI L. & FOÀ A. 1996. Seasonal variation of pineal involvement in the circadian organization of the ruin lizard *Podarcis sicula*. *Journal of Experimental Biology* 199: 1189-1194.
- INNOCENTI A., MINUTINI L. & FOÀ A. 1993. The pineal and circadian rhythms of temperature selection and locomotion in lizards. *Physiology and Behavior* 53: 911-915.
- ISABEKOVA S.B., TLEPBERGENOVA L.N. & VESELKIN N.P. 1987. Central connections of the parietal eye of the lizard. *Journal of Evolution, Biochemistry and Physiology* 23: 258-263 (in Russian).
- JANIK D.S. & MENAKER M. 1990. Circadian locomotor rhythms in the desert iguana. I: The role of the eyes and the pineal. *Journal of Comparative Physiology (A)* 166: 803-810.
- JENISON G.L. & NOLTE J. 1980. An ultraviolet-sensitive mechanism in the reptilian parietal eye. *Brain Research* 194: 506-510.
- JONES S.M. 1989. A thermographic study of temperature regulation in the lizard. *Lacerta vivipara*. Ph.D. Dissertation, University of Bristol, U.K.
- JOSS J.M.P. 1978. A rhythm of hydroxyindole-O-methyltransferase (HIOMT) activity in the scincid lizard *Lampropholis guichenoti*. *General and Comparative Endocrinology* 36: 521-525.
- KENNAWAY D.J., FRITH R.G., PHILLIPOU G., MATTHEWS C.D & SEAMARK R.F. 1977. A specific radioimmunoassay for melatonin in biological tissues and fluids and its validation by gas chromatography-mass spectrometry. *Endocrinology* 101: 119-127.

- KORF H.W. & WAGNER U. 1981. Nervous connections of the parietal eye in adult *Lacerta s. sicula* Refinesque as demonstrated by anterograde and retrograde transport of horseradish peroxidase. *Cell and Tissue Research* 219: 567-583.
- KOSH R.J. & HUTCHISON V.H. 1972. Thermal tolerance of parietectomized *Anolis carolinensis* acclimated at different temperatures and photoperiods. *Herpetologica* 28: 183-191.
- LANGLOIS J.P. 1902. La regulation thermique chez les poikilothermes. *Journal de Physiologie et de Pathologie Générale* 4: 249-256.
- LEVEY I.L. 1973. Effects of pinealectomy and melatonin injections at different season on ovarian activity in the lizards *Anolis carolinensis*. *Journal of Experimental Zoology* 185: 169-174.
- LICHT P. & PEARSON A.K. 1970. Failure of parietectomy to affect the testes in the lizard *Anolis carolinensis*. *Copeia*: 172-173.
- MAHAPATRA M.S., MAHATA S.K. & MAITI B.R. 1986. Circadian rhythms in serotonin, norepinephrine, and epinephrine contents of the pineal-paraphyseal complex of the soft-shelled turtle (*Lyssemys punctata punctata*). *General and Comparative Endocrinology* 67: 279-281.
- MAHAPATRA M.S., MAHATA S.K. & MAITI B.R. 1988. Circadian rhythms and influence of light on serotonin, norepinephrine, and epinephrine contents of the pineal-paraphyseal complex in the soft-shelled turtle (*Lyssemys punctata punctata*). *General and Comparative Endocrinology* 71: 183-188.
- MCKEEHAN A. & SIEVERT L.M. 1996. The effect of shielding the parietal eye of *Podarcis muralis* on behavioral thermoregulation. *Journal of Thermal Biology* 21: 397-401.
- MENAKER M. 1985. Eyes - the second (and third) pineal glands?, pp. 78-92. In: Evered D. & Clark S., Edits. Photoperiodism, melatonin and the pineal. *London: Pitman*.
- MENAKER M. & TOSINI G. 1996. The evolution of vertebrate circadian system, pp. 39-52. In: Honma K. & Honma S., Edits. Circadian organization and oscillatory coupling. *Sapporo: Hokkaido University Press*.
- MENAKER M. & WISNER S. 1983. Temperature compensated circadian clock in the pineal of *Anolis carolinensis*. *Proceedings of the National Academy of Science, U.S.A.* 80: 6119-6122.
- MENDONCA M.T., TOUSIGNANT A.J. & CREWS D. 1995. Seasonal changes and annual variability in daily plasma melatonin in the red-sided garter snakes (*Thamnophis sirtalis parietalis*). *General and Comparative Endocrinology* 100: 226-237.
- MENDONCA M.T., TOUSIGNANT A.J. & CREWS D. 1996a. Pinealectomy, melatonin and courtship behavior in male red-sided garter snakes (*Thamnophis sirtalis parietalis*). *Journal of Experimental Zoology* 274: 63-74.
- MENDONCA M.T., TOUSIGNANT A.J. & CREWS D. 1996b. Courting and non-courting male garter snakes (*Thamnophis sirtalis parietalis*): plasma melatonin and the effects of pinealectomy. *Hormones and Behavior* 30: 176-185.
- MEYER J. & BROOKS G.R. 1968. Effect of blinding and parietectomy on color change in *Anolis carolinensis* (Reptilia: Iguanidae). *Virginia Journal of Science* 19: 122-125.
- MILLER W.H. & WOLBARSH M.L. 1962. Neural activity in the parietal eye of lizard. *Science* 135: 316-317.
- MISRA C. & THAPLIYAL J.P. 1979. Time of administration of indolamines and testicular response of Indian garden lizard *Calotes versicolor*. *Indian Journal of Experimental Biology* 17: 1383-1385.
- MOLINA-BORJA M. 1996. Pineal-gland and circadian locomotor activity rhythm in the lacertid *Gallotia galloti eisentrauti*, pinealectomy induces arrhythmicity. *Biological Rhythm Research* 27: 1-11.
- MOYER R.B., FIRTH B.T. & KENNAWAY D.J. 1995. Effect of constant temperatures, darkness and light on the secretion of melatonin by pineal explants and retinas in the gecko *Christinus marmoratus*. *Brain Research* 675: 345-348.
- NELSON R.J., MASON R.T., KROHMER R.W. & CREWS D. 1987. Pinealectomy blocks vernal courtship behavior in red-sided garter snake. *Physiology and Behavior* 39: 231-233.
- OWENS D.W., GERN W.A. & RALPH C.L. 1980. Melatonin in the blood and cerebrospinal fluid of the green sea turtle (*Chelonia mydas*). *General and Comparative Endocrinology* 40: 180-187.

- PACKARD G.C. & PACKARD M.J. 1972. Photic exposure of the lizard *Callisaurus draconoides* following shielding of the parietal eye. *Copeia*: 695-701.
- PALENSCHAT D. 1964. Beiträge zur locomotorischen Aktivität der Blindschleiche (*Anguis fragilis* L.) unter besonderer Berücksichtigung des Parietalorgans. *Ph.D. Dissertation, Georg-August Universität, Göttingen, Germany*.
- PETIT A. & VIVIEN-ROELS B. 1977. Les rythmes circadiens et circannuels du taux de 5-hydroxytryptamine (serotonine) chez *Lacerta muralis* Laurenti (Reptiles-Lacertiliens). *Archives de Biologie* 88: 217-234.
- PHILLIPS J.A. & HARLOW H.J. 1981. Elevation of upper voluntary temperatures after shielding the parietal eye of the horned lizards. *Herpetologica* 37: 199-205.
- PHILLIPS J.A., HARLOW H.J. & RALPH C.L. 1980. Set-point shifts of behavioral thermoregulation in horned lizards after parietal eye manipulation. *American Zoologist* 20: 732.
- PHILLIPS J.A. & HOWES K.A. 1988. The pineal complex, aggressive behavior and thermoregulation in curly-tailed lizards, *Leiocephalus carinatus*. *Physiology and Behavior* 42: 103-108.
- PICKARD G.E. & TANG W.X. 1993. Individual pineal cells exhibit a circadian rhythm in melatonin secretion. *Brain Research* 627: 141-146.
- QUAY W.B. 1979. The parietal eye - pineal complex, pp. 245-406. In: Gans C. et al., Edits. *Biology of the Reptilia 9, Neurology A*. London: Academic Press.
- RALPH C.L., FIRTH B.T. & TURNER J.S. 1979. The role of the pineal body in ectotherm thermoregulation. *American Zoologist* 19: 273-293.
- RIDGEWAY P.M. & KENT G.C. 1971. Effects of parietectomy and blinding on the testes of the lizard *Anolis carolinensis*. *American Zoologist* 11: 651.
- RISMILLER P.D. 1987. Thermal biology of *Lacerta viridis*: seasonal aspects. *Ph.D. Dissertation, Philipps-Universität, Marburg, Germany*.
- RISMILLER P.D. & HELDMAIER G. 1987. Melatonin and photoperiod affect body temperature selection in the lizard *Lacerta viridis*. *Journal of Thermal Biology* 12: 131-134.
- ROTH J.J., GERN W.A., ROTH A.C., RALPH C.L. & JACOBSON E. 1980. Nonpineal melatonin in the alligator (*Alligator mississippiensis*). *Science* 210: 548-550.
- ROTH J.J. & RALPH C.L. 1976. Body temperature of the lizard (*Anolis carolinensis*): effect of parietectomy. *Journal of Experimental Zoology* 198: 17-28.
- SAARELA S. & REITER R.J. 1994. Function of melatonin in thermoregulatory processes. *Life Sciences* 54: 295-311.
- SIEVERT L.M. & HUTCHISON V.H. 1989. The parietal eye and thermoregulatory behavior of *Crotaphytus collaris* (Squamata: Iguanidae). *Comparative Biochemistry and Physiology* 94A: 339-343.
- SKENE D.J., VIVIEN-ROELS B. & PEVET P. 1989. Pineal 5-methoxytryptophol rhythms in the box turtle: effect of photoperiod and environmental temperature. *Neuroscience Letters* 98: 69-73.
- SKINNER D.C. 1991. Effects of intraperitoneal melatonin injections on the thermoregulation in the Transvaal girdled lizard, *Cordylus vittifer*. *Journal of Thermal Biology* 16: 179-184.
- SOLESSIO E. & ENGBRETSON G.A. 1993. Antagonistic chromatic mechanisms in photoreceptors of the parietal eye of lizards. *Nature* 364: 442-445.
- SONGDAHL J.H. & HUTCHISON V.H. 1972. The effect of photoperiod, parietectomy and eye enucleation on oxygen consumption in the blue granite lizard *Sceloporus cyanogenys*. *Herpetologica* 28: 148-156.
- STEBBINS R.C. 1960. Effects of pinealectomy in the Western Fence Lizard *Sceloporus occidentalis*. *Copeia*: 276-283.
- STEBBINS R.C. 1963. Activity changes in the Striped Plateau Lizard with evidence on influence of the parietal eye. *Copeia*: 681-691.
- STEBBINS R.C. 1970. The effect of parietectomy on testicular activity and exposure to light in the desert night lizard (*Xantusia vigilis*). *Copeia*: 261-270.
- STEBBINS R.C. & COHEN N.W. 1973. The effect of parietectomy on the thyroid and gonads in free-living western fence lizards (*Sceloporus occidentalis*). *Copeia*: 662-668.
- STEBBINS R.C. & EAKIN R.M. 1958. The role of the "third eye" in reptilian behavior. *American Museum Novitates* 1870: 40.

- STEBBINS R.C. & WILHOFF D.C. 1966. Influence of the parietal eye on activity in lizards, pp. 258-268. In: Bowman R.I., Edit. Galapagos: Proceedings of the Symposia of the Galapagos International Scientific Project. Berkeley: University of California Press.
- TILDEN A.R. & HUTCHISON V.H. 1993. Influence of photoperiod and temperature on serum melatonin in the diamondback water snake, *Nerodia rhombifera*. *General and Comparative Endocrinology* 92: 347-354.
- TOSINI G. 1993. Thermoregulation in the lizard *Podarcis muralis*: application of thermography and similar infra-red technologies. *Ph.D. Dissertation, University of Bristol, U.K.*
- TOSINI G. & AVERY R.A. 1993. Intraspecific variation in lizard thermoregulatory set points: a thermographic study in *Podarcis muralis*. *Journal of Thermal Biology* 18: 19-23.
- TOSINI G. & AVERY R.A. 1994. Occlusion of the parietal eye induces a transient wavelength-dependent shift in a lizard thermoregulatory set points. *Journal of Experimental Zoology* 269: 84-87.
- TOSINI G. & AVERY R.A. 1996. Spectral composition of light influences thermoregulatory behaviour in a lacertid lizard (*Podarcis muralis*). *Journal of Thermal Biology* 21: 191-195.
- TOSINI G., FOÀ A. & AVERY R.A. 1996. Pinealectomy increased thermoregulatory set points in the lacertid lizard *Podarcis sicula*. *Journal of Herpetology* 30: 104-106.
- TOSINI G. & MENAKER M. 1995. Circadian rhythm of body temperature in an ectotherm (*Iguana iguana*). *Journal of Biological Rhythms* 10: 248-255.
- TOSINI G. & MENAKER M. 1996. The pineal complex and melatonin affects the daily rhythm of temperature selection in the green iguana. *Journal of Comparative Physiology (A)* 179: 135-142.
- TUREK F.W. & VAN CAUTER E. 1994. Rhythms in reproduction, pp. 487-450. In: Knobil E. & Neil J.D., Edits. Physiology of reproduction. New York: Raven Press.
- UNDERWOOD H. 1973. Retinal and extraretinal photoreceptors mediate entrainment of the circadian locomotor rhythm in lizards. *Journal of Comparative Physiology* 83: 187-222.
- UNDERWOOD H. 1977. Circadian organization in lizards: the role of the pineal organ. *Science* 195: 587-589.
- UNDERWOOD H. 1979. Melatonin affects circadian rhythmicity in lizards. *Journal of Comparative Physiology* 130: 317-323.
- UNDERWOOD H. 1981. Circadian organization in the lizard *Sceloporus occidentalis*: the effects of pinealectomy, blinding and melatonin. *Journal of Comparative Physiology* 141: 537-547.
- UNDERWOOD H. 1983. Circadian organization in the lizard *Anolis carolinensis*: a multioscillatory system. *Journal of Comparative Physiology* 152: 265-274.
- UNDERWOOD H. 1985a. Extraretinal photoreception in the lizard *Sceloporus occidentalis*: phase response curve. *American Journal of Physiology* 248: R407-R414.
- UNDERWOOD H. 1985b. Annual testicular cycle of the lizard *Anolis carolinensis*: effects of pinealectomy and melatonin. *Journal of Experimental Zoology* 233: 235-242.
- UNDERWOOD H. 1990. The pineal gland and melatonin: regulators of circadian function in lower vertebrates. *Experientia* 46: 120-128.
- UNDERWOOD H. 1992. Endogenous rhythms, pp. 229-297. In: Gans C. & Crews D., Edits. Biology of the Reptilia. Hormones, brain, and behavior. Vol. 18. Chicago & London: The University of Chicago Press.
- UNDERWOOD H. & HARLESS M. 1985. Entrainment of the circadian activity rhythm of a lizard to melatonin injection. *Physiology and Behavior* 35: 267-270.
- UNDERWOOD H. & MENAKER M. 1970. Extraretinal light perception. Entrainment of the biological clock controlling lizards locomotor activity. *Science* 170: 190-193.
- UNDERWOOD H. & MENAKER M. 1976. Extraretinal photoreception in lizard. *Photochemistry and Photobiology* 23: 227-243.
- VIVIEN-ROELS B. 1983. The pineal gland and the integration of environmental information: possible role of hydroxy- and methoxyindoles. *Molecular Physiology* 4: 331-345.
- VIVIEN-ROELS B. 1985. Interaction between photoperiod, temperature, pineal and seasonal reproduction in non-mammalian vertebrates, pp. 187-209. In: Mess B. et al., Edits. The pineal gland: current state of pineal research. Amsterdam: Elsevier.

- VIVIEN-ROELS B. & ARENDT J. 1979. Variations circadiennes et circannuelles de la mélatonine épyphysaire chez *Testudo hermanni* G. (Reptile-Chelonien) dans des conditions naturelles d'éclairage et de température. *Annales d'Endocrinologie, Paris* 40: 93-94.
- VIVIEN-ROELS B. & ARENDT J. 1981. Relative roles of environmental factors, photoperiod and temperature in the control of serotonin and melatonin circadian variations in the pineal organ and plasma of the tortoise *Testudo hermanni*, Gmelin, pp. 401-406. In: Birau N. & Schloot W., Edits. Melatonin: current status and perspectives. *New York: Pergamon Press*.
- VIVIEN-ROELS B. & ARENDT J. 1983. How does the indoleamine production of pineal gland respond to variation of the environment in a non-mammalian vertebrate, *Testudo hermanni*, Gmelin. *Psychoneuroendocrinology* 8: 327-332.
- VIVIEN-ROELS B., ARENDT J. & BRADTKE J. 1979. Circadian and circannual fluctuations of pineal indoleamines (serotonin and melatonin) in *Testudo hermanni* Gmelin (Reptilia, Chelonia) I. Under natural conditions of photoperiod and temperature. *General and Comparative Endocrinology* 37: 197-210.
- VIVIEN-ROELS B., PEVET P. & CLAUSTRAT B. 1988. Pineal and circulating melatonin rhythms in the box turtle, *Terrapene carolina triunguis*: effect of photoperiod, light pulse, and environmental temperature. *General and Comparative Endocrinology* 69: 163-173.
- VIVIEN-ROELS B., PEVET P., DUBOIS M.P., ARENDT J. & BROWN G.M. 1981. Immunohistological evidence for the presence of melatonin in the pineal gland, the retina and the Harderian gland. *Cell Tissue Research* 217: 105-105.