The Regulation of Circadian and Circannual Biorhythm by Pineal Body. The Finestructure, Innervation and Cytochemical Evaluation of Pineal Body in Human and Different Vertebrates

PhD thesis

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Introduction

The corpus pineale has an important role in the development of **circadian and circannual** life rhythm. The normal daily rhythm of the individual organs are basically controlled by self-regulating „slave clocks" dictating the diurnal rhythm for 24 hours. The daily rhythm of the different organs is coordinated by the hypothalamic nucleus suprachiasmaticus (the „master clock"). Their coordinated operation are adjusted to the biotypical illumination relations existing in different parts of the Earth by non-visual photoreceptors, mainly by the corpus pienale.

Formation of the pineal hormon, melatonin, is hindered by light, thus the most melatonin is produced at night and in winter. Among other effects, melatonin has also an antigonadotrop effect, which influences the operation of the hormon system and regulates thereby the daily and seasonal rhythm of the organism. Artificial lights in night hinders the production of pineal melatonin, which may have pathological effects, such as breast cancer in women or colorectal carcinoma in men.

Aims of the work

There are very few data known about the fine structure of human corpus pineale due to the lack of quick fixation possibilities needed for electronmicroscopic investigations (Fejér et al, 1989, Vígh et al. 2003). In the literature, the study of corpus pineale occurs mainly in different experimental animals, but as this raises fundamental pathological aspects in humans, a detailed *comparative* study is justified concerning the fine structural and immunocytologic investigations presented in this work.

An accurate study of the fine structure is made necessary also by the fact that new results showed a *nerve tissue* nature of the organ, in contrast to statements in former investigations which supposed a glandular tissue structure of it.

At starting the studies, practical X-ray investigations had a very significant role in the diagnosis of cerebral processes. This is based on the good imaging possibilities for the acervulae sitting in the corpus pineale, what helps the early diagnosis of expansing pathological processes. This subject motivated the study of pineal *calcification.*

In knowing a more accurate fine structure and afferentation-efferentation phenomena, determination of the chemical components of pineal organs is also important for understanding their function. For this purpose, immuno-cytochemical investigations were also performed, and a comparison of pineal organs of different species and their retinal photoreception was also carried out. In *histochemica*l studies, besides of the molecules playing role in their photochemical operation, determination of the mediating materials of neural afferentation and efferentation was the further goal of our investigations.

In the literature, reduction in the light transmission capacity of the skull of mammals and humans contributed to the development of the regression theory of pineal light perception. For clarifying this problem, comparison was performed between the light transmission capacity of the *skull.* We studied the role of *autonomous fibres* in innervation.

Methods

Immunocytochemical investigations

After embedding, we carried out electron microscopic investigation of the immunoreaction against **GABA**, **glutamate** and **aspartate.** We also used **retinal opsin** antiserum, **pinopsin** antibodies, and monoclonal antidotes **OS-2, Cos-1**, as well as **cryptochrom** antidote. Depending on embedding and fixation, the primary antiserum was used in a dilution from 1 : 500 to 1 : 5000.

Study of pineal light afferentation

In studying pineal afferentation, we investigated the mediation of vegatative fibres in retinal afferentation as supposed in the literature. For recognizing vegetative fibres, we applied

tyrosine hydroxylase reaction by using polyclonal and monoclonal antidotes.

In another group of studies, we investigated the light transmission capacity of skulls, mainly in humans, by comparing it in different ages. In this subject arose also the study of pineal calcification, for which, besides its clinical significance, we emphasized also the relationship of calcification with light perception.

Species studied

In addition to humans, different kinds of species were examined, mammals, birds, reptiles, amphibia, osteichthyes and chondrichthyes, cyclostomata. for comparing the pineal organs of **submammalia** having well-developed pineal light perception and **pineal organs of mammals** to be known as regressive.
Following species were studied:

Mammals: Cercopithecus aetiops, Rhesus macacus (monkies), laboratory rats, mice, cats, northern opossum, Didelphys virginiana, Erinaceus roumanicus, Sorex araneus, Putorius furo, Mustela vison, Martes foina, Orictolagus cuniculus,
From among *bats:* Myotis blythi oxygnatus, Rhinolophus ferrum equinum, Taphozous longimanus, Scotophylus hethai, Pteropus temmincki, Cynopterus sphinx, Rousettus niloticus (egypticus).

Bird species: Gallus domesticus, Numida meleagris, Phasianus cochicus, Coturnix coturnix japonica, Meleagris gallopavo; Columba livia; Anser anser; Anas platyrhynchos, Passer domesticus; Taeniopyga guttata, Turdus merula; Turdus viscivorus; Serinus canaria; Parus major; parotts, Melopsittacus undulatus; Buteo buteo; Struthio camelus.

Reptiles: Lacerta viridis; Lacerta agilis, Lacerta muralis, Iguana iguana,Teratoscincus scincus, Phelsuma laticauda angularis; Emys orbicularis; Pseudemysscripta elegans; Anolis carolinensis; Phelsuma laticauda; Iguana iguana; Natrix natrix; Natrix tesselata; Elaphe longissima.

Amphibia: Triturus cristatus; Triturus punctatus; Pleurodeles waltlii; Salamandra maculosa; Amblystoma mexicanum; Bombina bombina; Bombina variegata; Pelobates fuscus; Rana esculenta; Rana arvalis; Bufo bufo; Bufo viridis; Xenopus laevis; Hyla regilla.

Osteichthyes: Cyprinus carpio; Phoxinus phoxinus; Salmo gairdneri; Carassius auratus; Anguilla anguilla.

Chondrichthyes: Raja clavata; Scyliorchinus canicula; Chimaera monstrosa.

Cyclostomata : Lampetra planeri.

Results

Comparative morphology

Before our investigations, there were no data on the fine structure of the pineal organ of human adults. Electron microscopic studies of the organ proved that the corpus pineale develops from epithalamus, it is not of peripherial gland, but it is a brain tissue with retinal character, which is formed from cone-type photoreceptor pinealocyta, secondary pineal neurons and glial cells. Therefore we don't use the usual name „pineal gland", instead of this, we call it „pineal organ" showing thereby also for people not dealing with this subject directly that the organ is not of gland, but a part of the nerve tissue.

Construction of mammalian pineal organ

The fine structure of pinealocytes of mammals are the same as that of the human ones. Only in some mammals show differenciated photoreceptor structures characteristic for inferior species, in their majority the outer segment is represented by specific sensory cilia. Part of the pinealocytic axons form a neurohaemal nerve terminal on the vascular surface of the organ. Another part of the axons form synapses of ribbon content on pineal neurons, what corresponds to the connection between retinal photoreceptors and bipolar neurons.

In *bats,* we performed a more detailed comparison of corpus pineale and the retina. The retina of microchiropteran species seems to correspond to the reduced importance of visual eyesight originating from the night way of living. The undeveloped retina of megachiropteran species cannot be suitable for recieving the image projected on it about the outside world and for indicating the objects of the outside world as a locator. Therefore we suppose that this „retina-structure of a corpus pinealic-like nature" serves mainly for measuring the light intensity, just like photometers, similarly to the pineal organ in these species.

The pineal organ of birds

In the last four decades, more than 700 articles appeared in the literature about the pineal organ of birds, but only few data are known about the fine structure of this organ. Thus, in our work, we wanted to provide detailed data about the construction of it obtained via light- and electron microscopic investigations.

In the species studied by us, the pineal organ is situated immediately under the skull and it is bound to epithalamus by a long pineal stalk. The wall of the organ has sack-like bulges, and as it is developed from the tegmental part of the third ventricle, its outside surface is covered by diencaphalic pia mater and arachnoid membrane. The meninx penetrates deeply into the organ along the recesses, but it is always separated from the pineal nervous tissue by a basal membrane.

Similarly to neurons, pinealocyta are of bipolar nature: the have receptor and effector apophyses, the receptor process is of dendritic nature, its terminal, a thickened part, forms an inner segment similar to the retinal cones and rods. The effector processes are of axon nature, and they end either on the secondary pineal neurons, or they form neuro-hormonal terminals on the surface of the pineal nerve tissue. Not only pinealocytic axon terminals are to be found on neurons, but also axon terminals differing from their ribbon-type endings, which may act as interneuronal connections or pinealopetal afferentation.

In the pineal meninges, the vegetative fibres – similarly to mammals – do not terminate on pineal cells, but on blood vessels of the organ, forming vasomotoric terminals.

Pineal organs of reptiles

In the species studied, two types of pineal organs exist, corpus pineale and parietal eye.

The **corpus pineale** is situated intracranial, and it is lobulated. It is connected to the epithalamus by habenulae, pineal apophyses. Pinealocytes have differentiated photoreceptor

outer segments, their axons form ribbon-containing synapses on the pineal neurons. In the pineal organ of reptiles the vegetative nerve fibres end also around the blood vessels.

The **parietal eye** consists of a dorsal lens and a ventral retina, above which the transparent „cornea" part of the skull is situated. The bubble-like organ is not lobar, but its cytological structure is similar to that of the pineal organ. The cornea on the top above the parietal eye makes for the light possible to enter the organ, whereas light can arrive to the corpus pineale only through the skull, in a significantly filtered quality.

It is known that reptiles reside often on biotopically sunny areas for regulating their body temperature. It is supposed that the different light perceptions of the two kinds of their pineal organs perform, on the one hand the perception of the daily or seasonly change of the light rhythm (corpus pineale), and on the other hand, they help in visiting the sunny aereas for the regulation of the body temperature of reptiles (parietal organ).

Pineal organs of Amphibia

In our work, we studied frog species among Amphibia, in which a pineal organ and a frontal eye exist.

The **frontal eye** or forehead eye is smaller than the corpus pineale, it is situated outside the skull, in the skin of the top, on the area between and above the eyes. The skin part covering the organ is pigment-free, fully transparent and it has no colour-filtering property. Among photoreceptors, both rods and cones exist, their axon-like apophyses end on the nerve tissue of the organ by ribbonic synapses. The axons of neurons, as „forehead nerve" are connected from the pineal to the habenular, pretectal and tegmental brain stem regions and to the nerve fibres going to the hypothalamic periventricular area.

The **pineal organ** of frogs is larger than the forehead eye, it is situated belov the skull top, more caudal than the front eye. There are light percepting cells of rod and cone nature, the axons of which end on the pineal neurons. In terminals, besides synaptic vesicules and granular vesicules, synaptic ribbons can also be found. The fibres form also neuro-hormonal

nerve terminals. This means the discharge of pineal neuro-hormons, among them that of melatonin, as local hormons. The transparent skull part above the organ also may help the discovering of sunny areas.

The most significant characteristic of the pineal organ of frogs is the presence of different photoreceptor, they will be investigated in the chapter of immuno-cytochemistry.

Pineal organs of fishes

In **osteoichthyes**, the external parts of their photoreceptor pineal organs are lifted into the lumen of the organ which is a continuation of the recessus pinealis of the third ventricle. The pineal neurons, similarly to the secondary neurons of the retina, percept the light information of the phtoreceptor pinealocytes, and forward it via the tractus pinealis.

The structure of the **parapineal organ** is similar, but the differentiation of their individual elements is lower than that of the cells of the corpus pineale.

In sharks and rays belonging to the species of **chondrichthyes** no parapineal organ is present. The pineal organ is differentiated in the form of a longer tube, where the duplicity of the organ is indicated by proximal and distal expansion. The photoreceptor pinealocytes are mainly of rod nature, and synaptize with two kinds of glutamate-erg neurons. The axons of neurons form the tractus pinealis, they end in the praetectal area of the thalamus, on the nerve cells of the tuberculum posterius, further in the tegmentum mesencaphali and in the GnRh neurons of the mesencephalon.

In our investigations we compared the differentiation of the external parts of photoreceptors with more developed species, and we found them more differentiated in lower species. Significant number of dendrites can be observed in the lumen and in the pineal recess of the third ventricle of the organ. For teh dendrites is characteristic that they have ciliary endings, similarly to the liquorcontacting neurons in the cerebral ventricle.

Cyclostomata

In the **Lampetra** species the pineal organs are represented by the corpus pineale and the parapineal organ. Both the pineal organ and the parapineal organ consist of photoreceptor cells and secondary neurons, besides of ependymal cells. The pineal organ is situated immediately below the skull, whereas the parapineal sensing organ is in a deeper position.

The membrane system of of the external parts of pineal photoreceptor cells is well developed and show an explicit rhodopsin immun-reactivity (see in the immuno-cytochemical chapter).

Cytochemical investigations

Molecules playing a role in the photoreception of pineal organs (1), mediator materials in pineal afferentation and efferentation (2) and pineal calcification (3) have been studied by cytochemical methods. Among molecules playing a role in the photoreception, retinal (A) and pineal (B) opsines have been investigated.

Study of retinal opsines in pinealocytes

We studied chondrichthyes and cyclostomata. We performed light microscopic immuno-reactive studies in Raja clavata, which gave positive results in the outer segments.

Similarly, the outer segments of pineal photoreceptor cells in the cyclostomata Lampetra fluviatilis gave positive rhodopsine immunoreaction.

Localization of pinopsine

We found reactions with pinopsine-specific antibodies in the outer segments of pinealocytes in numerous bird species. According to the measurement of absorption maxima, these photoreceptors are green-blue sensitive. Most emphasized was the pinopsine immunopositivity in the big pinealocytes of lizard species, the small pinealocytes showed marks with O2S antibodies.

Rod-like pinealocytes of frogs showed a pinopsine immunoreaction.

Study of synaptic mediators

As mediators, excitatoric amino acids: glutamates and aspartates, and the inhibitory GABA have been studied.

In mammals, small-size pineal neurons give the GABA immuno-reaction and they form GABA-erg terminals on pinealocytes and large-size neurons. The axonal terminals of pinealocytes give the glutamate immunoreaction on the large-size pineal neurons.

In reptiles, the axon-like apophyses of pinealocytes give a glutamate immunoreaction, in the first line, the synaptic ribbons.

In Amphibia, the pinealocytes contained both, glutamate and aspartate on their synaptic ribbons.

The axon-type apophyses of pinealocytes form glutamate immuno-reactive terminals on the dendrites of pineal neurons. Axons of the pineal neurons form the glutamate immuno-reactive pineal tract.

In the pineal and parapineal organs of the Cyclostomata, *Lampetra fluviatilis*, immuno-reactive amino acids can also be detected.

The glutamate immunoreaction is strongest in the presynaptic terminals of photoreceptors and secondary neurons. Similar phenomenon is known also for the retina, therefore it can be supposed that the excitatoric amino acids have a similar synaptic mediator role in the pineal organs, as in the retina.

Pineal calcification

Sections made from pineal organs for light microscopic investigations were stained by the Kossa reagent for calcium detection. For electron microscopic purposes, we used the pyroantimonate method for calcium detection. This latter method makes free Ca-ions visible by precipitating them in the form of Ca-pyroantimonate, as well-localized, electrondense particles.

In human samples – in accordance with the literature - we could establish that the number of pineal concrements is larger in older persons. Human pineal acervuli were also studied by scanning electron microscope, in which study the spatial position of acervuli can be well observed.

Pineal acervuli can be found in numerous mammals as well, in such as monkeys, cattle, horses, donkies, sheep, guinea-pigs, Mongolian running mice, minks, rats and bats. As a control, the sections were decalcinated with EDTA, then these particles loosed their electrodense material, proving that they were really calcium particles.

By applying the pyroantimonate method, Ca-accumulation could be shown in the retina, along the photoreceptor cell membranes.

Comparing mammals with submammals, acervulus formation could only be shown **in birds**. In the corpus pineale of adult geese, brain sand (acervulus cerebri) could be found which had similar structure as in mammals, mainly in meningeal position.

In the outer segment of the photoreceptors **in amphibia,** a big number of Ca-pyroantimonate particles are precipitated, mainly in the outer segments of the rod-like type. This localization is the same as that of Ca-pyroantimonate reaction in the outer segments of the retina.

The pineal afferentation of light information

The light receptors of pinealocytes, the outer segments of their photoreceptors are reduced during evolution, decreasing thereby the light transmission of the skull. The question arises,

how the light information controls the function of pineal organs in more developed living beings?

One of the possibilities is the fibre-afferentation coming from the retina. The other question is, whether light is capable of reaching the organ through the skull?

Vegetative pineal afferentation

We studied vegetative afferentation supposed in the literature (Korf, 1995) in numerous species. In all the species, vegetative fibres arrive into the corpus pineale along blood vessels from its meningeal capsule, and come into the inside of the organ in the interfollicular meningeal septa of the organ. Most of the fibres are unmyelinated, but there are among them also some myelinated fibers. Nerv fibres arrive not only along the arterien feeding the corpus pineale, but also along veines from where blood is flowing into the cerebral veins (*nervus conarii*).

Following these nerves by serial sections, we can see that they do not enter into the pineal nerve tissue, but remain in the meningeal septum, and form there nerve terminals on the nonstriated muscle cells of pineal arterioles. In the terminal part of axons there are numerous synaptic and granular vesicles.

Both the periarteriolar and perivenal fibres show the *tyrosine hydroxilase* reaction. The present studies show the **vasomotoric nature** of vegetative fibres on the terminals ending on pineal blood vessels. Tyrosine-hydroxilase immunoreactive fibres are of vasoconstrictor nature, whereas the negative ones of vasodilator or of vasosensoric nature. Similar function was already mentioned by earlier scientists (Holmgren, 1917; Quay et al.; 1968; Owman and Rüdeberg, 1970; Reuss and Schröder, 1988; Moller and Baeres, 2002). Thus we think that the experimentally found role of vegetative fibres in the pineal operation can be explained not by the conduction of retinal light information, rather by **the vascular supply** of tissue activity.

Retinal light information arriving into the corpus pineale via habenules by central fibres may rather be supposed from the viewpoints of nerve tissue science and physiology. Vasomotoric terminals were found not only in mammal corpus pineale but also in submammalians having a developed light perception.

Light transmission capacity of human skull and that in different vertebrates

In literature, human and mammal skulls are considered as not light transmitting, and the regression of pineal light perception is supposed contrasted to the light percepting pineal organs of submammalians. We found in our earlier work that numerous light transmitting area exist on the skulls not only in some experimental vertebrates, but also in humans. In our experiments, we irradiated the skulls of humans and some mammals (monkey, cat, rat, guinea-pig, rabbit) with a lamp of 60 W light light intensity in order to detect their light transmission capacity.

Strongest light transmitting capacity of the skull was detected in newborns, mainly in the area of the fontanelles. Attention of parents should be called that babies should sleep in darkness also during the day for helping the production of melatonin.

In adults, the foveolae granulares and the sulcus arteriae madiae show the strongest light transmitting property. The number of Pacchioni granules is larger in older skulls. Transparent are also the sinus sagittalis superior, the scaly part of the skull's frontal parietal and occipital area, the ducts of the emissarium veins and several other individual transparent areas on the different parts of the calvaria. In leading the light to the corpus pineale, a role is also played by the liquor cerebrospinalis.

The present experimental results should be taken into account for of people working on night duty or in working in more shifts, where in addition to lack of sleeping, the reduction in the illumination of the skull can decrease further the already reduced melatonin content.

Conclusions

The construction of corpus pineale in humans and different vertebrates

The light microscopic and electron microscopic study of serial sections of human corpus pineale show that the pineal tissue is the continuation of the epithalamic nerve tissue. Corpus pineale develops from epithalamic evaginations. Therefore the pineal organ is a part of the brain and cannot be considered as a glandular tissue.

Cytochemical investigation of the corpus pineale

Immuno-cytochemical studies testify also against the glandular nature of pineal tissue, because molecules known in the retinal phototransductional cascades could be detected in it. Photoreceptor molecules can be found not only in cyclostomata, fishes and amphibias, but also in reptiles, birds and mammals, even in human corpus pineale. The pinopsine immunoreaction in mammals was detected only in a lower degree. The photoreceptors detected develop the circadiane and circadian rhythm of the organ through the production of pineal melatonin.

Pineal calcification

In our experiments, free calcium-ions could be detected ultrastructurally by potassium pyroantimonate along the cell membranes in human corpus pineale, which justifies the role of membranes in the formation of acervuli. Intrapineal acervuli show a globular surface, whereas those in arachnoid are in form of heller and darker concentric rings. Heller rings contain more calcium than the darker ones. The number of the largest layers is in correlation with age.

Pineal calcium konkrements of mammals are mainly of the meningeal type. In rats on which parathyroidectomy has been performed, more and larger acervuli can be found. This indicates the role of parathyroid regulation in the calcium household and the formation of acervuli.

In most submammalians the structure of pineal organs (corpus pineale, parapineal organ, frontal eye, parietal eye) is similar to that of the retina. Acervuli could be detected only in the corpus pineale of some birds.

In thin-walled retina and in the similar structure of the corpus pineale of submammalians, the diffusion of extracellular calcium is supposedly free, in contrast to the larger and more compact pineal tissue of mammals, where the local concentration of calcium may be larger.

Efferentation and afferentation of corpus pineale

Electron microscopic studies show that in the corpus pineale of birds there are more neurohormonal terminals than in that of mammals. In the course of evolution, birds evolved paralelly with mammals, therefore – against the general opinion – they cannot be considered a transition from reptiles to mammals.

Concerning pineal efferentation, it should be emphasized that the effector pole of pinealocytes is formed by an axonal apophysis, which either forms a synapse on secondary pineal nerve cells, or it terminates as a surface neurohaemal ending. In pigeons, a serotine immunoreaction could be detected in the granular visiculae of the surface terminals. In these terminals also interactive asparatate and glutamate could be found. Excitatoric amino acids have a specific regulating effect in the hormonal efferentation of the neurohypophysis, what can be expected in pineal hormonal efferentation as well.

It should be emphasized that it is well known from the literature that the melatonin secretion hindered by night illumination is the main endocrine factor causing pathologic phenomena (Kayumov et al., 2005; Reid and Zee, 2004; Copinschi, 2005; Navara and Nelson, 2007; Brainard et al., 2008; Blask, 2009; Folken et al., 2010; Haldar and Ahmad, 2010).

As the experiments showed the role of sympathical nerves in the daily rhythm of pineal melatonin formation, it was supposed that at the regression of pineal photoreception, light information is mediated by vegatative fibres from the retina (Wurtman et al., 1964;Romijn,

1975; Bowers et al., 1984; Reiter, 1991; Moore, 1996; Somoneaux and Ribelayaga, 2003; Mukuda et al., 2009). In our studies, the vegetative fibres ended on blood vessels, thefore they can influence melatonine formation as vasomotoric regulatory fibres.

The **light transmission capacity of human skulls** is most intense in newborns, corresponding to the property of the fontanelles. The fonticulus major calcificizes in the second year of life, the other fonticula later. This period of life is very important from the viewpoint of the development of daily and seasonal rhythms.

In adults, light goes through the skull at Pachioni granules, at the cavities of menengial arteria, at the area of the sinus and on the occipital squama.

In half of the human skulls studied, there **are also individual transparent areas** which may cause individual differences in the pineal melatonin production. In people working at night it is justified to examine preventively the light transparency of the skull.

In **the mammals** studied the whole area of the skullcap is transparent.

In **reptiles and Amphibia**, above the pineal organs well defined bone tissue-free transparent areas of the skull and pigment-free skin areas are to be found.

In case of **fishes**, one has to take into account the light filtering effect of water acting mainly in the region of short wavelengths.

Based on our investigations it can be suggested that in night shifts, in addition to the red eye-glasses filtering out the light of short wavelengths – the skull should also be covered, especially in case of thin and hell hair, for decreasing the pathological consequences of melatonin secretion.

We also suggested in the lighting at night shifts to reduce the short wavelength illumination, against which pineal metonine formation is extremely sensitive.

Summary

Construction of corpus pineale in humans and different vertebrates

The investigation of serial sections of **human corpus pineale** by light and electron microscopy showed that the organ is in continuous connection with the epithalamus, it could not be considered to be a glandular tissue, but it is a nervous tissue: it is not a „pineal gland", but it is a **pineal organ**.

Pinealocytes in **mammals** have a fine structure similar to that of human ones. In *bats*, we compared in detail the structure of the corpus pineale and retina. The retina of megachiroptera species is plicate, it cannot be suitable for accepting the image projected from the outside world in an umbrella-like manner. Thus we suppose that in this species it serves not for seeing, rather for measuring light intension, just like the pineal organ.

In **submammalians,** the so-called pineal complex is formed by two organs developed from the tegmen of the diencephalon: in reptiles the corpus pineale and the parietal eye, in frog species the pineal organ and the frontal organ (frontal eye), in cyclostomata and osteichthyes the pineal and the parapineal organ. We suppose that the two organs originate from the conjugate dorsal diencephalic eye of more ancient Vertebrates.

Cytochemical study of corpus pineale

Photoreceptor molecules are present not only in cyclostomata, fishes and amphibia, but also in the corpus pineale of reptiles, birds and mammals.

Our electron microscopic studies show that in the corpus pineale of birds more neurohormonal terminals can be found than in mammals, thus their corpus pineale is more active in secretion than that of mammals. In the large and plicate pineal organ of more differentiated species, the number of pinealocytes is larger, and in addition, the longer activation time of the pinopsine molecule in it also may increase light sensitivity.

Efferentation and afferentation of the corpus pineale

In all, humans, mammals and more primitive vertebratae there are pineal neurons on which the axons of pinealocytes terminate. Axons of neurons run into the habenular nucleus through the stem of corpus pineale. Part of the pinealocytic axons form a neurohormonal nerve terminal on the vascular surface of the organ, serving for the secretion of pineal hormons. No vegetative nerve fibres terminate on the pinealocytes, they don't enter into the pineal nerve tissue, but they terminate on blood vessels serving the regulation of the movement of the blood vessels. Central fibres are also to be found in the pineal nerve tissue, they may transmit afferentation into the organ.

Corpus pineale obtains light information through the skull as well, mainly in submammalians, but also in humans. In humans, until the closing of fontanelles, the entering of light is obvious, but light can get into the skull also via the sulci arteriosi and the foveolae granulares.

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