Review Article

Pineal gland - A mystic gland

Daniel Silas Samuel[1], Revathi Duraisamy[1], M. P. Santhosh Kumar[2]*

ABSTRACT

The pineal gland has been the subject of amazement and awe down the centuries. The structure and function of this enigmatic gland play an important role in day-to-day life of human beings. The pineal gland secretes an important hormone melatonin which is necessary for lightening the skin tone, and it has several other important functions in humans. The pineal gland is composed mainly of pinealocytes. The pineal gland is present in the midline of the skull and is a part of epithalamus and hypothalamus. It regulates the secretion of both. The pineal gland is activated by darkness and it is mandatory to maintain a normal circadian rhythm of sleep-wake cycle, if not humans may turn into zombies. The pineal gland is also present in animals. The secretion of this gland in higher amounts causes precocious puberty and development of primary and secondary sexual characters mainly in boys. It is also called the third eye since after eye, and it is the only gland which detects light but, on the contrary, secretes melatonin largely under darkness. This gland also affects the mood of human beings, thereby getting involved in the psychological behavior of men. It increases the immune action of human beings; thereby, it also acts as immunostimulant preventing a person from attack of antigen by producing a suitable antibody. Its presence hinders the spread of tumor and becomes malignant, and its calcification affects the memory or the memorizing capacity of the brain leading to dementia. This article reviews the anatomy and physiology of the pineal gland and the various functions of melatonin in humans.

KEY WORDS: Melatonin, Mystic gland, Pineal gland, Sleep-wake cycle

INTRODUCTION

The pineal gland has tremendous control over the homeostatic mechanisms of the body. Melatonin produced by it regulates circadian rhythm, sleep-wake cycle, thermal and immunologic systems, menstrual and reproductive irregularities, psychological and behavioral disorders, and tumor inhibition. Melatonin receptors present in the brain, retina, and pituitary and elsewhere produce certain biological effects in human beings.

ANATOMY

The pineal gland is a calcified structure present in the midline of the plain skull [Figure 1], shaped like a pine cone as seen in X-rays.[1] It develops from the neural crest cells of the roof of diencephalon. It is attached to the posterior roof of the third ventricle, between posterior commissure and the more dorsal habenular commissure.[2]

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Arterial Supply

The arterial supply to the pineal gland is from the posterior choroidal arteries including quadrigeminal, thalamic and posterolateral branches derived from the cerebral arteries that course through the posterior aspect of mesencephalon.[3]

Venous Drainage

It drains through short-course veins into the straight sinus and empties into the internal cerebral veins and basal veins of Rosenthal, which forms the great cerebral vein of Galan.[4] The veins and arteries often enter pineal tissue through vascular hila as paired vessels [Figure 2].[5]

Neural Innervation

It begins at the retina to the suprachiasmatic nuclei (SCN) through the retinohypothalamic tract. Each SCN receives bilateral retinal projection contralaterally with most fibers crossing over at optic chiasma.[6] It synapses at the lateral hypothalamus, within the brain stem, from where descending projections pass through intermediolateral column of cord, from which

[1]Department of Prosthodontics, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India, [2]Department of Oral and Maxillofacial Surgery, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India

***Corresponding author:** Dr. M. P. Santhosh Kumar, Department of Oral and Maxillofacial Surgery, Saveetha Dental College,Saveetha Institute of Medical and Technical Sciences, Saveetha University, 162, Poonamallee High Road, Velappanchavadi, Chennai - 600 077, Tamil Nadu, India. Phone: +91-9994892022. E-mail: santhoshsurgeon@gmail.com

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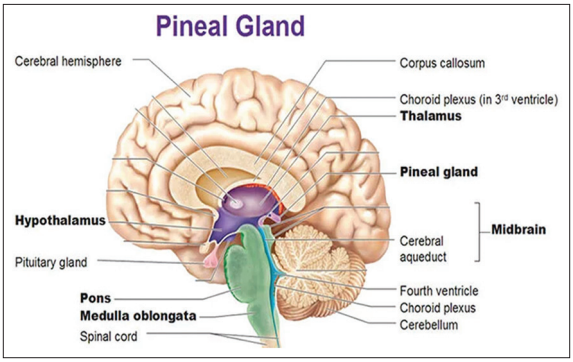

Figure 1: Anatomy of the pineal gland

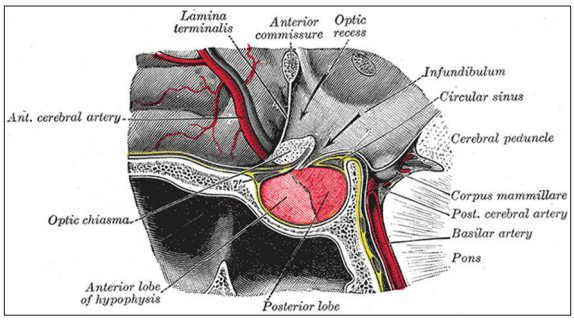

Figure 2: Arterial and blood supply of the pineal gland

preganglionic fibers reach the superior cervical ganglion (SCG). Post-ganglionic noradrenergic fibers from SCG reach the pineal gland through nervi conarii which, in turn, pass through tentorium cerebella [Figure 3].[7]

HISTOLOGY

The pineal body consists of a lobular parenchyma of pinealocytes (also known as pineocytes) surrounded by connective tissue spaces and the interstitial cells (also known as supportive cells). It may be of glial origin and is covered by a layer of pial capsule. As it is made up of both cortex and white matter, it may be mistaken for a neoplasm. It consists mainly of pinealocytes [Figure 4].[8] The human pineal gland grows within the age of 1–2 years, remaining stable thereafter, although its weight increases gradually from puberty onward. Deposits of the calcite form of calcium carbonate are met within it. The reason for aging of a person is because of the calcium and phosphorus deposits that it has been enriched with. Calcification of the pineal gland is typical in adults and has also been observed in children. The pineal gland is not isolated from the body by the blood–brain barrier system because it produces profuse blood flow, second to the kidney.

LOCATION

The pineal gland is reddish-gray and about 5–8 mm in humans. It is located beneath the stria medullaris, between the laterally positioned thalamic bodies just rostrodorsal to the superior colliculus.[9] It is part

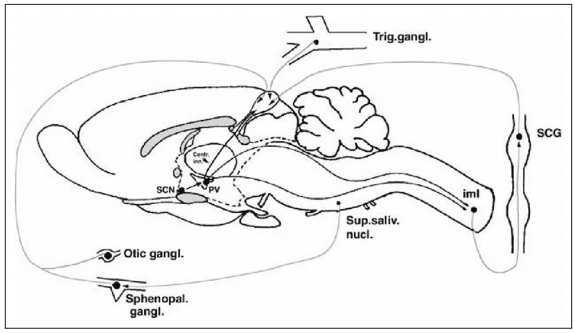

Figure 3: Neural innervation of the pineal gland

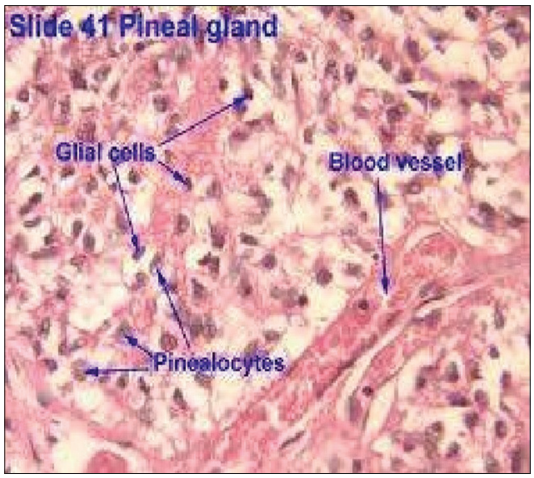

Figure 4: Histology of pineal gland

of the epithalamus. To observe the pineal, cerebral hemispheres should be reflected laterally and then to be looked for a small grayish bump in front of the cerebellum.

Comparative Anatomy

Pinealocytes seen in many non-mammalian vertebrates have a strong resemblance to the photoreceptor cells present in the eye. Ancestor retinal cells share a common characteristic to the vertebral pineal cells. Exposure to light can set off a chain reaction and enzymatic events within the pineal gland that regulates circadian rhythms in some vertebrates. Some early vertebrate fossil skulls have a pineal foramen. The lamprey and the tuatara and some of the vertebrates that have a parietal organ or "third eye" are photosensitive. The third eye represents evolution of earlier approach to photoreception.[10] The structures of the third eye in the tuatara are comparable to the cornea, lens, and retina, of a vertebrate retina. The brain of the Russian Melovatka bird is about 90 million years old, and it shows a larger-than-expected parietal eye and pineal gland.

Biosynthesis of Pineal Hormones

Pinealocytes synthesize two different types of substances, namely indoles and polypeptides. Melatonin or 5-methoxy N-acetyl tryptamine, the major hormone of the pineal gland, was first isolated by Lerner in

1958. The biosynthesis begins with the conversion of the amino acid tryptophan into 5-hydroxytryptophan (5-HTP) by enzyme tryptophan hydroxylase. Decarboxylation of 5-HTP by 5-HTP decarboxylase gives rise to 5-hydroxytryptamine (5-HT) or serotonin. It was N-acetylated to form N-acetyl serotonin by enzyme serotonin N-acetyl transferase which was the rate-limiting enzyme in the biosynthesis of melatonin.[11]

N-acetyl serotonin was methylated to form melatonin by the enzyme hydroxy indole 0-methyltransferase. It was found to be present in the pineal gland and retina. The cofactors involved were S-adenosyl methionine, S-adenosyl homocysteine, and pteridines.

REGULATION OF SECRETION

The secretion of melatonin, the major pineal hormone, is rhythmic in nature, with high levels occurring in the night and low levels during the day. The rhythm is largely endogenous in nature. The suprachiasmatic nucleus (the "master circadian clock") present in hypothalamus is largely responsible for it. An increased release of norepinephrine from sympathetic neurofibers in nighttime increases the rate of synthesis of melatonin in pineal gland.

Melatonin inhibits the secretion of the gonadotropic hormones, luteinizing hormone, and follicle-stimulating hormone from the anterior pituitary, which, in turn, is due to inhibition of gonadotropin-releasing hormone from the hypothalamus, which is necessary for secretion of anterior pituitary hormones.[12]

FUNCTIONS OF PINEAL GLAND

The pineal gland was found to be a "vestigial remnant" of a larger organ. In 1917, it was known that extract of cow's pineal lightened frog skin. Dermatology professor Lerner *et al.* isolated a hormone and named it melatonin. The substance did not prove to be helpful as intended. Melatonin is N-acetyl-5-methoxy-tryptamine, a derivative of the amino acid tryptophan, and also functions on the central nervous system. The secretion of melatonin by the pineal gland is stimulated by darkness and inhibited by light. Removing the rats' pineal accelerated the ovary growth. Keeping rats in constant light decreased the weight of their pineal. The abundant melatonin levels in children are believed to hinder sexual development, and pineal tumors have been linked with precocious puberty. When puberty arrives, melatonin secretions are reduced in the body. The secretions of the pineal gland hinder the development of the reproductive glands because, in cases of severely damaged children, the result is accelerated development of the sexual organs and the skeletal structure.[13] Chordates have a close resemblance to the pineal cytostructures.

Some recent studies show that the degree of pineal gland calcification is significantly higher in Alzheimer's disease patients than the patients suffering from dementia. Pineal gland plays a role in the production of dimethyltryptamine (DMT) in the human brain. A massive release of DMT from the pineal gland before death can result in a near death experience.[14] All tumors involving the pineal gland are rare. A pineal tumor compresses the superior colliculi of the dorsal midbrain, producing Parinaud's syndrome. Pineal tumors also can cause compression of the cerebral aqueduct, resulting in a non-communicating hydrocephalus.[14]

Pineal gland participates in the physiological regulation of sleep and sleepiness. Melatonin along with phototherapy is used to treat sleep disorders. Their levels are low in elderly insomniacs relative to age-matched non-insomniacs. The amount of melatonin is higher in the spinal cord than in bloodstream which, in turn, controls the circadian rhythm-sleep and wake cycle. The gland secretes more antioxidant at the night, in absence of light, which helps to dictate someones sleeping pattern. In dark months of the winter, seasonal affective disorder has been due to low melatonin levels. Aside from the eyes, the pineal gland is the only organ that detects light.[15]

A low level of melatonin leads to human mood disorders, and it plays an important role in determining longevity and in the modulation of immune system functions. Maestroni and Conti (1991) proposed the existence of melatonin-immuno-opioids network with a physiological function providing a correct immune recovery after the depression caused by elevated corticosteroids is seen in stressful situations. Maestroni (1993) suggested that melatonin can be used as immunotherapeutic agent for immunodeficiency such as in conditions where melatonin is most active and indicated in acquired immunodeficiency syndrome (AIDS), i.e., CD4+ lymphocytes for both HIV and melatonin which could be helpful before the development of AIDS, when the T-helper lymphocytes function normally.[16]

ELECTROMAGNETIC ENVIRONMENT AND PINEAL GLAND

Light inhibits melatonin synthesis within the pineal gland. However, visible light constitutes only a very narrow portion of the total electromagnetic spectrum which varies from a very short high energy ionizing radiation such as X-rays, ultraviolet rays to an extremely low frequency , and long waves with energy so low that is incapable of extracting electrons from atom (non-ionizing electromagnetic waves).

Experiments on laboratory rodents have demonstrated that unusual electric, magnetic, or electromagnetic fields induce a reduction of melatonin synthesis and secretion, through an inhibition of N-acetyltransferase activity, a key enzyme responsible for the circadian rhythm of melatonin. A diminished melatonin message or perturbed circadian rhythm may, in turn, have a significant physiological consequence, including diminished antioxidant activity and anticancer protection. On the other hand, the exposure of rat brain occipital region to static magnetic fields resulted in a significant immunopotentiation.[17]

MYSTICISM, METAPHYSICS AND PHILOSOPHY, AND PINEAL GLAND

The secretory activity of the pineal gland is only partial as it is located deep in the brain. It suggested to philosophers that it is a "mystery" gland with mystical, metaphysical, and occult theories surrounding its perceived functions. René Descartes has called it the "principal seat of the soul" and believed that there was a point of connection between the intellect and the body. Descartes believed that it was a single section of the brain which existed as a single part, rather than two parts. Descates argued that because a person can never have more than one thought at the same time, external stimuli must be united within the brain before being revealed to the soul. He considered the pineal gland to be situated in the most suitable place for this purpose, located centrally in the brain, and surrounded by branches of the carotid arteries.[18]

Numerous spiritual philosophies contain the notion of an inner third eye that is related to the ajna chakra and the pineal gland, which is significant in mystical awakening or enlightenment, clairvoyant perception, and higher states of consciousness. This idea occurs in contemporary theories relating to yoga. The notion of a "pineal-eye" is central to the philosophy of the French writer Georges Bataille. It was considered as an organ in excess and delirium. According to Romijin, the pineal gland is the natural tranquilizing organ, the morphological substrate of the "seventh chakra," and the gateway to perfect harmony and rest.[19]

CONCLUSION

The pineal gland is a small midline structure under the brain which is not extensively studied. It secretes melatonin. Its main function is to suppress sexual growth in children. Its influence into metaphysics and mysticism is in the realm of polemic.

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