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Pineal Gland' Still a Bit of Mystery: An Escort Study

D.K. Sharma*, Vandana Sharma, Bikash C. Satapathy***, Manisha B. Sinha****, A.U. Siddiqui****, Soumitra Trivedi****, Mrithunjay Rathore******

Abstract

Some groups or communities believe that 'We literally have a third eye, which connects us to spiritual dimensions and supernatural forces' and it is claimed that the Pineal Gland (PG) is that third eye. Majority believes that PG is one of the endocrine glands in vertebrates and secretes mainly a hormone melatonin which regulates circadian rhythm or sleep cycle. In some lower vertebrates, PG has a well-developed eye like structure and in others if not organized as an eye, it functions like a light receptor. Neurobiological effects of meditation and mindfulness have been detected in the form of increased molecular levels of melatonin and dopamine. It is said that PG is relevant in medicine and healthcare for behavior change, stress regulation and treatment of addictions. Its deep location in brain suggested the philosophers throughout history that it possesses a particular importance. On the top of all, PG is also thought to secrete dimethyl tryptamine (DMT), a naturally occurring psychedelic compound called 'The Spirit Molecule' during dreaming, spiritual and mystical experiences and at the time of death. The role of PG as an endocrine gland and its secretory activity is poorly understood. Pineal gland's full purpose is still a bit of mystery and yet to be known but researchers suggest that we are getting closer to understanding PG and more about the entire endocrine system.

Keywords: Neurobiological Effects; Melatonin; Circadian Rhythm; Pineal; Psychedelic.

Introduction

Apart from 3rd eye PG has also been described as 'the seat of the soul', 'the part of the body in which the soul directly exercises its functions', 'the intuition organ', 'the connection point between body and spirit', 'the centre at which the soul and body interact and we receive messages from the divine' and so on. The synonyms of PG are pineal body, conarium and epiphysis cerebri. The PG is a small endocrine gland in the vertebrate brain which produces melatonin, a serotonin derived hormone, and affects the modulation of sleep patterns in both seasonal and circadian rhythms [1,2]. In shape it resembles a pine cone, hence its name and is located in the epithalamus near the center of the brain, between the two cerebral hemispheres, in a groove where the two halves of the thalamus join.

Nearly all vertebrates possess PG with the exception of Hagfish (the most primitive type of vertebrate)[3]. In Hagfish, there is a "pineal equivalent" structure in its dorsal diencephalon [4]. The Lancelet Branchiostoma Lanceolatum (the nearest existing relative to vertebrates) also lacks a recognizable PG. Few more vertebrates including the Alligator lack PG, as they have been lost in the course of evolution [5]. However the Lamprey, almost as primitive as Hagfish possesses PG [3]. In many reptiles, PG is represented by a combined structure with its anterior part pineal or parietal eye and posterior part glandular in nature. It is said that the human PG represents the persistent posterior glandular part only with the disappearance of anterior parietal eye.

So PG has a colorful and misunderstood history

Author's Affiliation: *Additional Professor,***Senior Resident, ****Assistant Professors, Department of Anatomy, All India Institute of Medical Sciences (AIIMS) Raipur Chhattisgarh India. **Associate Professor, Department of Anatomy, Gandhi Medical College, Bhopal Madhya Pradesh, India.

Corresponding Author: D.K. Sharma, Additional Professor, Department of Anatomy, All India Institute of Medical Sciences (AIIMS), Raipur-492 099, Chhattisgarh India.

E-mail: dhyanesh.sharma@gmail.com

and is considered a somewhat mysterious organ, as its function was discovered last of the endocrine glands. PG is compared to the photoreceptive 'third parietal eye' present in the epithalamus of some animal species, which is also called the pineal eye [6]. PG was once named 'the third eye' due to many reasons, ranging from its location deep central part of the brain to its connection with the light sensation. PG has been studied for thousands of years; during third century a famous Roman physician Galen described it as 'the seat of the soul'. This reference was given again by a prominent philosopher and mathematician Rene Descartes (1596-1650), who wrote about PG in depth. By supporting Galen's thoughts, Descartes commented that the PG is principal seat of the soul, where all our thoughts are formed however his observations have been widely rejected.

Anatomy: In adult human, PG is reddish-gray in color, about a grain of rice in size (5-8 mm), approximately 0.1 gram in weight. It is located just rostro-dorsal to superior colliculi, projecting posteroinferiorly between them, behind and beneath the stria medullaris between thalamic bodies. The gland is relatively larger in children but begins to shrink with the onset of puberty. It is a part of the epithalamus below the splenium of corpus callosum but separated from it by the tela choroidea of the third ventricle with location in the quadrigeminal or superior cistern or *cistern of the great cerebral vein and* so remains bathed in cerebrospinal fluid. A small pineal recess of the third ventricle projects into the stalk or peduncle of the gland to divide it anteriorly into two laminae, superior and inferior, containing the habenular and posterior commissure respectively. PG is a midline structure shaped like a pine cone [7,8].

Blood supply: PG has profuse blood supply, second to the kidney but distinct from most of the mammalian brain, because it is not separated from the body by the blood brain barrier system [9].

Innervations: PG has a rich supply of adrenergic nerves that greatly influence its function. Sympathetic innervation is from the superior cervical ganglion whereas parasympathetic from the pterygopalatine and otic ganglia. Further, some nerve fibers penetrate into the pineal gland via the pineal stalk as central innervation. The neurons in the trigeminal ganglion also innervate the gland with their nerve fibers containing the neuropeptide PACAP (pituitary adenylate cyclase-activating polypeptide).

Histology

Microscopically PG is composed of two types of cells, pinealocytes and neuroglial cells, with a rich network of blood vessels and sympathetic fibres derived from the superior cervical ganglion. No neural tissue is present and spaces or cysts may be present. Vessels and nerves enter the gland through the connective tissue septa which partly separate the lobules. Sympathetic ganglion cells may be present. PG presents a lobular parenchyma of pinealocytes surrounded by connective tissue spaces. The gland's surface is covered by a pial capsule. As it is quite cellular (in relation to cortex and white matter) it may be mistaken for a neoplasm [10]. PG consists mainly of pinealocytes but four other cell types have been identified (i) Pinealocytes are arranged in the form of cords and clusters among capillaries. Each cell consists of a cell body with 4-6 lengthy long tortuous cytoplasmic processes and stained lightly basophilic by special silver impregnation methods. Cytoplasmic processes end in relation to blood vessels as swellings having granules containing melatonin and its precursor serotonin. Pinealocytes are the main cell type forming 95% of the cell population. They are modified neurons characterized by large irregular nuclei and prominent nucleoli (ii) Interstitial cells are neuroglial cells mainly astroglial cells characterized by dark elongated nuclei with cytoplasm stained darker than that of the pinealocytes. They also have long cytoplasmic processes which support pinealocytes and blood vessels (iii) Perivascular phagocytes are antigen presenting cells, located close to capillaries in the gland (iv) Pineal neurons or sympathetic ganglion cells and (v) Peptidergic neuron-like cells possessing a paracrine regulatory function.

Calcareous concretions due to fluoride, calcium and phosphorus deposits are constantly present in the pineal after the 17th year of life in the form of aggregations called 'brain sand' or 'corpora arenacea or acervuli', which are basophilic bodies showing concentric layers and present extracellularly in the matrix and visible in x-rays of skull. Their number increases with the age and they serve as landmark to radiologists in. Chemical analysis shows that they are composed of calcium phosphate, calcium carbonate, magnesium phosphate, and ammonium phosphate [11]. Deposits of the calcite form of calcium carbonate were described in 2002 [12]. Calcium and phosphorus deposits in the PG have been linked with aging.

Development

PG grows in size until about 1–2 years of age and then remains stable [13,14] but its weight increases continuously from the puberty onwards [15,16]. It is believed that the rich levels of melatonin in children

inhibit sexual development. The PG tumors have been linked with precocious puberty. The melatonin production is gradually reduced after puberty.

Function

Melatonin production: PG has long been regarded as a vestigial organ of no importance but recent investigations have shown it as an endocrine gland of great importance producing hormone melanin mainly. The synthesis and discharge of melatonin is remarkably influenced by the exposure of animal to light and is more during dark period. Melatonin is N-acetyl-5-methoxy-tryptamine, a derivative of the amino acid tryptophan and it regulates the circadian rhythm or sleep cycle by contributing a person feeling awake or sleepy. The production of melatonin is stimulated by darkness and inhibited by light [17,18]. Photosensitive cells in the retina detect light and signal the suprachiasmatic nucleus (SCN), entraining its rhythm to 24-hour cycle in nature. Fibers project from the SCN to the paraventricular nuclei (PVN), relay the circadian signals to spinal cord and out via sympathetic system to superior cervical ganglia (SCG); and from there into PG. The compound pinoline is also produced in the pineal gland which is one of the beta-carbolines [19]. Apart from regulating circadian rhythm the melatonin has some other functions in central nervous system (CNS).

Regulation of other endocrine glands: Some scientists claim that melatonin blocks the secretion of gonadotrophins (LH and FSH) from the anterior pituitary gland. These hormones aid in the proper development and functioning of ovaries and testes. Studies on rodents suggest that PG influences the pituitary gland secretion of sex hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH). A pinealectomy was performed on rodents and no change in pituitary weight was observed however there was an increase in the concentration of FSH and LH within the gland. In this same study, administration of melatonin did not return the concentrations of FSH to normal levels, suggesting that pineal gland influences the pituitary glands secretion of FSH and LH through some other transmitting molecule. PG presents important regulatory influence on many other endocrine organs including the hypophysis cerebri, thyroid, parathyroid, adrenal and gonads [20].

Drug metabolism: Studies suggest that PG may influence the actions of recreational drugs like cocaine and antidepressants like fluoxetine (Prozac); and may protect against neurodegeneration.

Clinical Significance

Calcification: PG is typically seen in adults as becomes calcified and often seen in skull X-rays but has been observed in children as young as of 2 years. Calcification rates vary widely by country and correlate with an increase in age [21]. Internal secretions of PG inhibit the development of the reproductive glands, because in cases where it is severely damaged in children, the result is accelerated development of the sexual organs and the skeleton.[22] In animals, PG plays a major role in sexual development, hibernation, metabolism, and seasonal breeding. Some recent studies show that PG calcification is significantly higher in patients with Alzheimer's disease than other types of dementia. Calcification may contribute the pathogenesis of Alzheimer's disease and reflect an absence of crystallization inhibitors [23]. Calcium, phosphorus and fluoride deposits in PG have been correlated with aging, as the brain ages, more deposits collect [24].

Cancer: All tumors involving PG are occasionally seen and mostly arise from sequestered embryonic germ cells. They most commonly take the form of germinomas, similar to testicular seminoma or ovarian dysegerminoma. Most pinealophiles restrict the terms pinealoma to neoplasms arising from the pineocytes. Pineal tumor may compress the superior colliculi and pretectal area of the dorsal midbrain and results the Parinaud's syndrome. Pineal tumor also may compress the cerebral aqueduct and results the non-communicating hydrocephalus. These neoplasms are divided into two categories, pineoblastomas and pineocytomas on the basis of neoplastic aggressiveness. The manifestations of pressure effect consist of visual disturbances, headache, mental deterioration, and sometimes dementia-like behavior.

Other Animals

Pinealocytes in many non-mammalian vertebrates have a strong resemblance to the photoreceptor cells of eye. Some evolutionary biologists believe that the vertebrate pineal cells possess a common evolutionary ancestor with retinal cells. Pineal cytostructure seems to have evolutionary similarities to the retinal cells of chordates [25]. Modern birds and reptiles have been found to express the phototransducing pigment melanopsin in PG. Avian PG is believed to act like the SCN in mammals [26]. In some vertebrates, exposure to light can set off a chain reaction of enzymatic events within PG that regulate circadian rhythms [27]. Some early vertebrate fossil skulls have a pineal opening which correlates the physiology of the modern "living fossils", the lampreys and the

tuatara; and some other vertebrates having parietal eye, which is photosensitive. The parietal eye represents evolution's earlier approach to photoreception. The structures of pineal eye in tuatara are analogous to the cornea, lens, and retina, though the latter resembles that of an octopus rather than a vertebrate retina. The asymmetrical whole consists of the 'eye' to the left and the 'pineal sac' to the right. In animals that have lost the parietal eye, including mammals, the pineal sac is retained and condensed into the form of the pineal gland [28]. The brain of the Russian Melovatka bird, about 90 million years old, is an exception which shows a larger parietal eye and PG. In human and other mammals, the light signals necessary to set circadian rhythms are sent from the eye through the retinohypothalamic system to the SCN and PG.

Society and Culture

Seventeenth century philosopher and scientist Rene Descartes, dedicating much time to study PG, called it the 'principal seat of the soul'. Descartes attached significance to the gland because he believed it to be the only section of the brain to exist as a single part rather than one-half of a pair. He argued that, because a person can never have 'more than one thought at a time', external stimuli must be united within the brain before being considered by the soul, and he considered PG to be situated in the most suitable possible place for this purpose, located centrally in the brain and surrounded by branches of the carotid arteries [29]. Dutch philosopher Baruch Spinoza criticized Descartes viewpoint for neither following from self-evident premises nor being clearly and distinctly perceived as Descartes previously asserted that he could not draw conclusions of this sort. Baruch questioned what Descartes meant by talking of the union of the mind and the body.

The notion of a 'pineal-eye' is central to the philosophy of the French writer Georges Bataille, which is analyzed at length by literary scholar Denis Hollier in his study Against Architecture. In this work Hollier discusses how Bataille uses the concept of a 'pineal-eye' as a reference to a blind-spot in Western rationality and an organ of excess and delirium [30]. This conceptual device is explicit in his surrealist texts 'The Jesuve and The Pineal Eye' [31]. Many spiritual philosophies contain the notion of an inner third eye which is related to the Ajna chakra and PG; and is attributed significance in mystical awakening or enlightenment, clairvoyant perception and higher states of consciousness. This idea occurs historically in ancient central and eastern Asia, as well as in contemporary theories relating to yoga, theosophy, hinduism, pagan religion and New Age Spiritual Philosophies. In hinduism Lord Shiva with third eye shown on the median line superior to both the eyes; and a crescent moon placement with the Bindi, an ornament worn over the forehead are the outward marks indicating PG or Sixth or Ajana chakra.

History

PG was originally believed to be a 'vestigial remnant' of a larger organ. In 1917, it was known that extract of cow pineal lightened frog skin. Dermatology professor Aaron B. Lerner and colleagues at Yele Universily, hoping that a substance from the pineal might be useful in treating skin diseases, isolated and named the hormone melatonin in 1958 [32]. The substance did not prove to be helpful as intended but its discovery helped solve several mysteries such as why removing the rat's pineal accelerated ovary growth, why keeping rats in constant light decreased the weight of their pineals and why pinealectomy and constant light affect ovary growth to an equal extent; this knowledge gave a boost to the then new field of chronobiology.

Interpretation

The secretory activity of PG is only partially understood. Some believe that the pineal gland secretes a single hormone melatonin and its secretion is dictated by light. Researchers have determined that melatonin has two primary functions in humans i.e. controls circadian or biological rhythm and regulates certain reproductive hormones. Circadian rhythm is a 24-hour biological cycle characterized by sleep-wake patterns. Light exposure stops the release of melatonin and in turn helps control circadian rhythms. Melatonin secretion is low during the daylight hours and high during dark periods, which has some influence over our reaction to photoperiod i.e. the length of day versus night. Naturally, photoperiod affects sleep patterns but melatonin's degree of impact over sleep patterns is disputed.

What is fascinating is that PG actually has retinal tissue composed of photoreceptors rods & cones inside, just like the eye, and is wired to the visual cortex in the brain. The photoreceptors of the retina not only strongly resemble the cells of PG which even has vitreous fluid in it like the human eye. An article in Science News stated 'The retina and PG are the organs primarily responsible for the body's recognition and sophisticated processing of external light'. These two organs in mammals seemed to have little else in common and were consequently studied by separate groups of scientists but a new alliance of

researchers is now exploring striking similarities. Their findings suggest that PG was the evolutionary precursor to the modern eye. Furthermore, a study published in Experimental Eye Research revealed that 'Although the mammalian PG is considered to be only indirectly photosensitive, the presence of proteins in PG involved in photo transduction or light sensing in the retina, raises the possibility that direct photic events may occur in the mammalian PG'.

A circadian rhythm is a roughly 24 hours cycle in the physiological processes of living beings including plants, animals, fungi and cyanobacteria. In strict sense the circadian rhythms are endogenously generated and can be modulated by external cues such as sunlight and temperature. Circadian rhythms are physical, mental and behavioral changes which follow a roughly 24-hour cycle. The study of circadian rhythms is called chronobiology. The 'master clock' which controls the circadian rhythms, consists of a group of nerve cells in the brain called SCN which contains about 20,000 nerve cells and is located in the hypothalamus, an area just above optic chiasms. Circadian rhythms can influence sleep-wake cycles, hormone release, body temperature and other important bodily functions. They have been linked to various sleep disorders like insomnia, obesity, diabetes, depression, bipolar disorder and seasonal affective disorders. The body's master clock or SCN controls the production of melatonin hormone which makes us sleepy by relaying information from the eyes to the brain. When there is less light, like at night, the SCN tells the brain to make more melatonin so we get drowsy.

Jet lag occurs when travelers suffer from disrupted circadian rhythms. When we pass through different time zones, our body's clock will be different from our wristwatch. For example if we fly in an airplane from Mumbai to Imphal, we lose 3 hours of time and when we wake up at 7am, our body still thinks it is 4 am, making us feel groggy and disoriented. Our body's clock will eventually reset itself but this often takes a few days. Scientists learn about circadian rhythms by studying humans or by using model organisms that have similar clock genes. Researchers control the subject's environment by altering light and dark periods and then look for changes in gene activity or other molecular signals. Understanding what makes biological clocks tick may lead researchers to managements for sleep disorders, jet lag and other health problems.

In a research study, Shantha Rajaratnam Professor of Psychology at Monash University found that the performance of athletes, depending on circadian rhythms vary during the day up to 26 percent. One's circadian rhythm or circadian phenotype is the internal cycle regulating the behavioral and physiological systems in the body, and is important for determining time of performance best for the athlete. If the players are having issues with sleep, then the adjustments can be made for enhancing both the quality as well as quantity of sleep.

In 1990s, a British scientist Jennifer Luke discovered that fluoride accumulates to strikingly high levels in the pineal gland but it is not yet known if fluoride accumulation affects PG function. Preliminary animal experiments found that fluoride reduced melatonin levels and shortened the time to puberty. Based on this and other evidence, the US National Research Council has stated that 'fluoride is likely to cause decreased melatonin production and to have other effects on normal pineal function, in turn may contribute to a variety of effects in humans'. *PG has highest levels of fluoride in body* as a calcifying tissue that is exposed to a high volume of blood flow and a major target for fluoride accumulation. In fact, the calcified parts of PG have the highest fluoride concentrations, higher than either bone or teeth. While the impacts of these fluoride concentrations in PG are not yet fully understood, studies have found that calcified deposits are associated with decreased numbers of functioning pinealocytes and reduced melatonin production as well as impairments in the sleep-wake cycle. It has been claimed that a child drinking fluoridated tap water looses 20 I.Q. points by the age of 6, as compared to a child that doesn't consume any. United States study claims that due to raised consumption of fluoride the children get puberty at the earlier ages and carry health consequences including a high risk of breast cancer. In animal studies**,** fluoride exposure causes a decrease in the amount of circulating melatonin and lead to an accelerated sexual maturation in females. Similar findings are reported in few more epidemiological studies on populations drinking fluoridated water, like the girls of fluoridated community reached puberty five months earlier.

Calcite micro-crystals in PG are similar to otolith / otoconia in human internal ear bone minerals[33]. EM fields: 60 Hz suppresses the activity of PG in our home, work place and outside and reduces melatonin production. These crystals expand and contract due to the presence of EM field of about 60 Hz normally present around us[34]. Pineal calcification is piezoelectric [35]. Piezoelectricity means electricity resulting from pressure or in response to the applied mechanical stress. This is in the frequency range of cell phone communication. Calcium crystals are capable of tuning into radio-stations without the use of electricity [36].

PG is said to secrete a chemical, dimethyl tryptamine (DMT) a naturally occurring psychedelic compound (a component of Ayahuasca-a plant medicine) which has the nickname of 'The Spirit Molecule'. DMT is believed to be released from the PG during dreaming, during spiritual and mystical experiences and during time of death. PG naturally makes its own DMT when fully operational and then creates a visionary state. Spiritual philosophies claim about supernatural forces and events which are hidden, neither apparent to the senses nor obvious to the intelligence. These supernatural forces and events can be seen, felt and heard by activating PG by Meditation. Neurobiological effects of Meditation and Mindfulness have been claimed in the form of increased molecular levels of melatonin and dopamine. Meditation may be relevant in medicine and healthcare to manage behavior change, stress regulation and addictions; and in its extended form the state of Buddhism or Enlightenment can be achieved.

Pineal detoxification or cleaning has also been claimed by avoiding (i) Fluoride (tooth paste, tap water) (ii) Organic foods (meat, pesticides etc) (iii) Alcohol and smoking (iv) Mercury (tooth fillings, vaccines, eating fish, eco light bulbs etc) (v) Heart Healing (overall vibration of the being and seeing other dimensions) (vi) Other toxins (artificial sweeteners, refined sugar, phylenanine in squashes, deodorants, cleaning chemicals, dental mouthwashes, air fresheners) which are really bad for the pineal gland. Raw chocolate / cacao is a pineal gland stimulant / detoxifier in high doses because of the high antioxidant content. Being disciplined with steps (i) to (vi) for a year or so will certainly bring about pineal cleaning and step (vii) is optional but very useful.

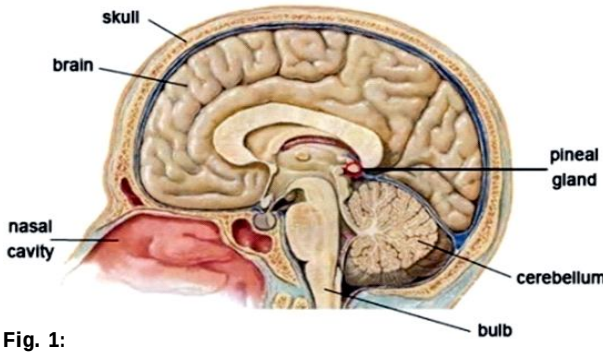


Fig. 1:

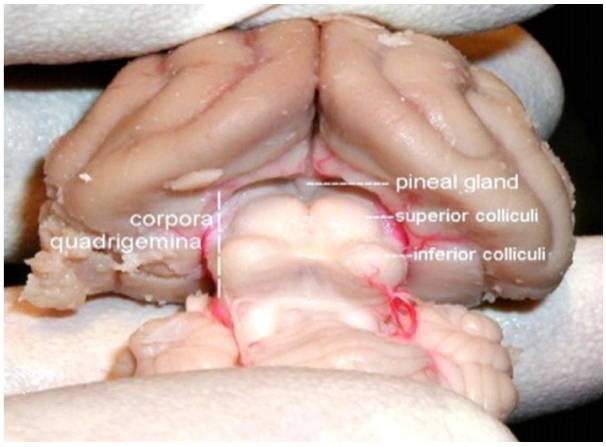
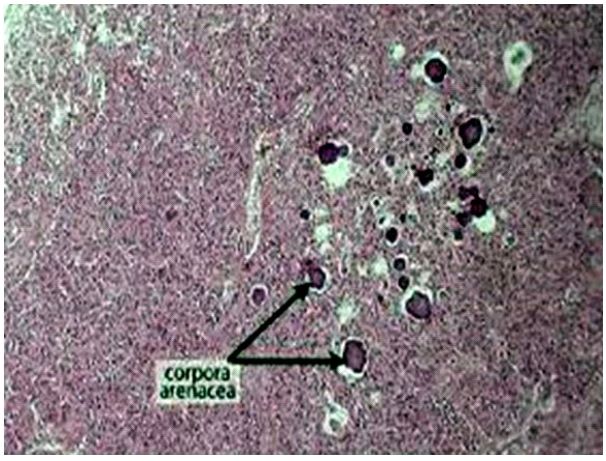


Fig. 2:



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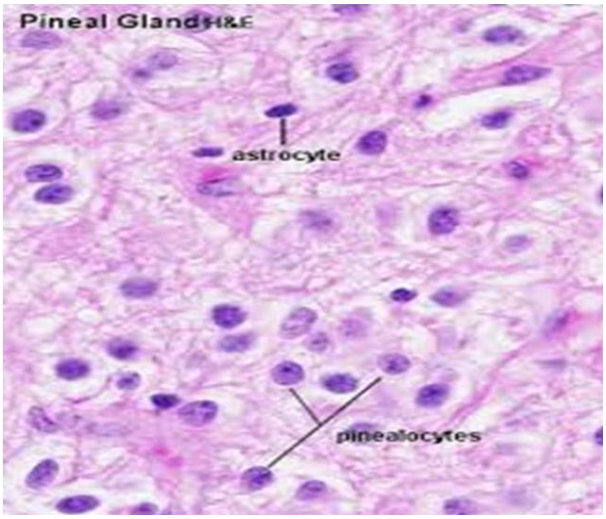

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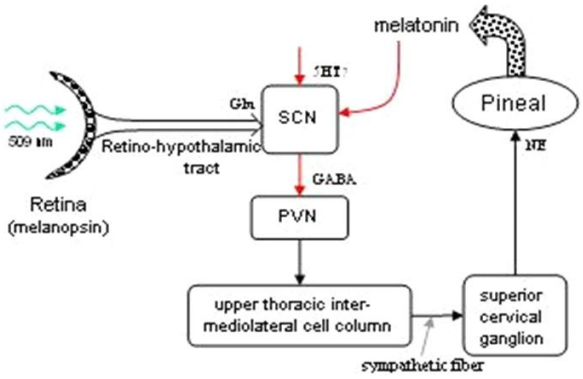

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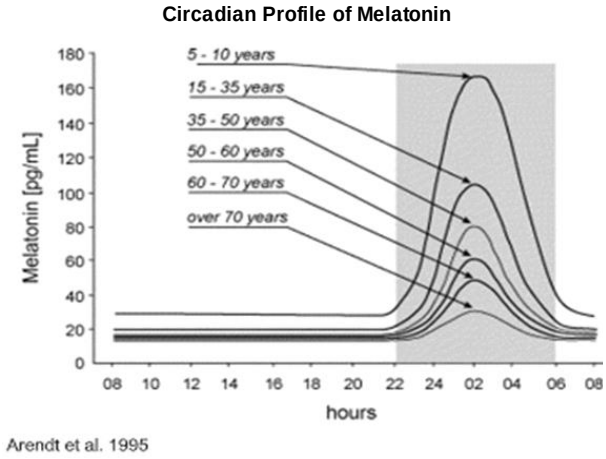

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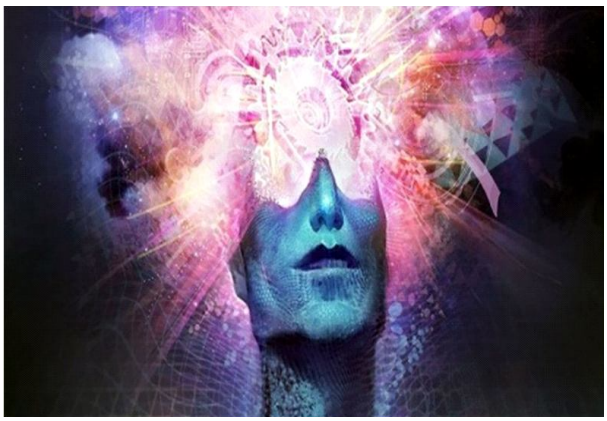

Fig. 7:

Fig. 8:

Fig. 9:

Long term effects of Melatonin is not known and it is not yet approved by Food and Drug Administration (FDA), even then it is being used in some country as anti aging or rejuvenating agent to boost vitality.

Conclusion

The pineal gland's full purpose is still a bit of a mystery. The role of pineal as an endocrine gland and its secretory activity is poorly understood. In humans, the function of melatonin is less well understood. Researchers are still learning about the full purpose of PG and suggest that we are getting closer to the complete understanding the pineal gland; and more about the endocrine system as a whole. Animal studies reveal that it secretes many neurotransmitters eg. melatonin, serotonin and norepinephrine; of these only melatonin is shown to be released into blood and can be considered as a true hormone. Attempt to demonstrate a functional link between PG and normal human processes have yielded equivocal and often confusing results. Its location deep in the brain suggested to philosophers throughout history that it possesses a particular importance. This combination leads it to be regarded as a gland with mystical, metaphysical and occult theories surrounding its perceived functions and so PG is still a bit of mystery.

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