PINEAL GLAND AND ITS PHYSIOLOGY

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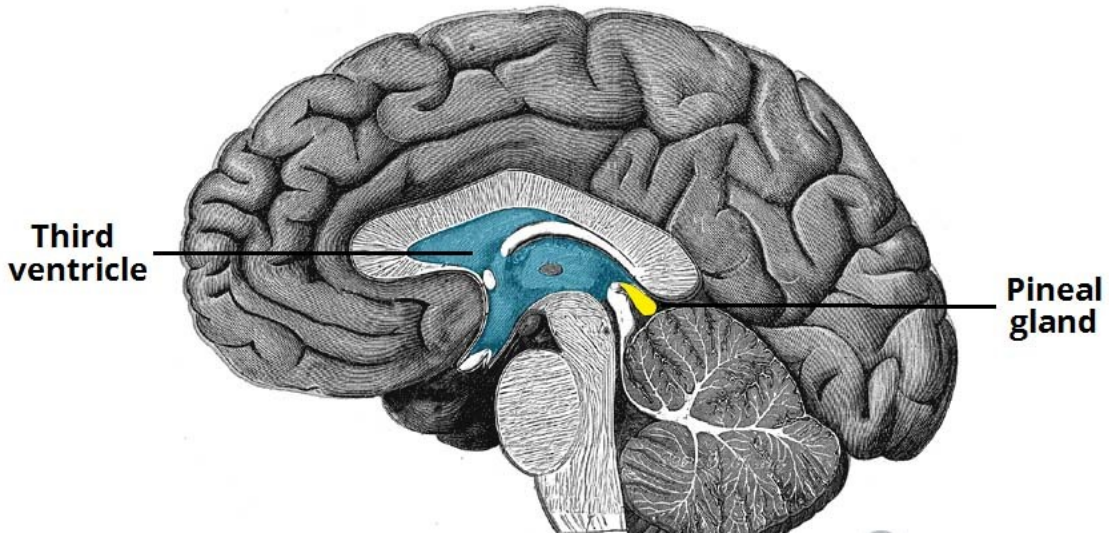
Pineal gland is so called because it resembles a "pine cone". Pineal was previously considered as vestigial organ, a remnant of 'third eye' without any significant function. Nowit is established that it secrets Melatonin[1].

Pineal gland is a small endocrine gland in the vertebratebrain. It produces serotonin derivative melatonin i.e. N,N-dimethyltryptamine[1].

Physiological anatomy: Its shape resembles a tiny pine cone (hence its name). it is located near the centre of the brain, between the two hemispheres.



Endocrine cells of pineal are called as Pinealocytes. Phylogenetically, pinealocytes are photoreceptors (light sensitive cells). These cells are arranged in cords & lobules. Cords are separated by connective tissue septa. Connective tissues can have calcium deposits called as PINEAL SAND. Calcified pineal can be located in X – rays[2].

Innervation:Sensory information from eye is important for regulation of pineal functions. Light suppresses pineal secretion whereas secretion increase in darkness. In humans and other mammals, the light signals necessary to set circadian rhythms are sent from the eye through the retinohypothalamic system to the suprachiasmatic nuclei (SCN) and then to pineal gland[3].

Factors affecting Melatonin secretion:

1. Light - dark cycle
2. Photo period
3. Age
4. Exercise
5. Stress
6. Electrical & magnetic field

Light – dark cycle:Melatonin secretion shows a circadian rhythm. Level higher at night (peak level at 3-4 am). Internal clock present in suprachiasmatic nucleus of hypothalamusmaintains circadian rhythmicity of melatonin[4].

Photo period: Relative duration of light & darkness is different during different months. During summers - the days (light period) are longer. During winter – nights (dark night) are longer. During winter when dark period is longer – duration of melatonin secretion is prolonged. In addition to circadian rhythm there is also annual rhythm such as; secretion is more during winters[5].

Age: Highest nocturnal levels seen at the age of 1 year; after which levels decline gradually. The human pineal gland grows in size until about 1–2 years of age, remaining stable thereafter. The abundant melatonin levels in children are believed to inhibit sexual development. When puberty arrives, melatonin production is reduced.

Exercise and stress: Acute vigorous exercise transiently increases melatonin secretion. Stress also increases melatonin. Melatonin, the indole produced at nighttime in pineal, has recognized anti-aging, anti-inflammatory, and anti-oxidant properties[6].

Physiological actions of Melatonin:

1. Effect on metabolic rate: Melatonin reduces metabolic rate in hibernating animals. Survival of hibernating animals in winters months depends on their ability to reduce their BMR. During hibernation in winter months, longer dark periods are there which would lead to more melatonin & less BMR[7].
2. Effect on reproduction: The pineal gland mediates the effect of photo period on reproduction. This is particularly important in seasonally breeding animals like goats & sheep[8]. In cold blooded animals in times of hibernation when melatonin secretion is more, reproduction is suppressed.

In humans, Melatonin suppresses gonadotropin secretion from the pituitary or it has anti gonadotropic action[9]. Human melatonin keeps the sexual maturation in check. This observation has been extended by Kitay, who has shown that destructive tumors of pineal gland are associated with precocious puberty whereas hyperactive tumors are associated with delayed puberty.

Two pineal indoles, melatonin and methoxytryptophol, have been shown to be antigonadotropic when administered to animals. When levels of these hormones measured in schoolchildren then findings show that in young boys there was an abrupt fall in the concentration of melatonin with advancing development suggesting that it may play an important physiological role in the control of human puberty[10].

3. Effect on body temperature: Melatonin affects body temperature. There is inverse relationship between Body temperature & melatonin circadian rhythm. In women Melatonin causes acute lowering of temperature[11].It also explains diurnal temperature rhythm in human being.
4. Effect on inflammation & immunity:Melatonin also possess anti inflammatory actions. Melatonin has been shown to reduce tissue destruction during inflammatory reactions by various means. Melatonin by virtue of its ability to directly scavenge the toxic free radicles reduces macromolecular tissue damage in all organs. The free radicals, reactive oxygen & nitrogen species scavenged by melatonin are – the highly toxic hydroxyl radical (OH), peroxynitrite anion (ONOO-), and hypochlorous acid (HOCl), among others. These all agents contribute to inflammatory reaction & associated tissue destruction. Moreover, Melatonin has other means to lower the damage associated with inflammatory reaction. It prevents the translocation of nuclear factor kappa – B (NF-kappa B) to the nucleus and its binding to DNA. In this way preventing the upregulation of variety of proinflammatory cytokines e.g. interleukins &tumor necrosis factor alpha. Finally, there are evidences suggesting that melatonin reduces the production of adhesion molecules that promote the sticking of leukocytes to the endothelial cells, thereby reducing trans endothelial migration of leukocytes &oedema which contribute to tissue damage[12, 13].

Pathophysiological implications of Melatonin

1. Jet lag: Jet lag commonly affects air travellers who travel across several time zones. It results when body's internal rhythm does not match with day – night rhythm of destination. Melatonin is used as a drug to re- align body's circadian rhythm with the outside world. Melatonin is very effective in reducing jet – lag. It can be recommended to adult travellers flying across five or more zones[14].
2. Sleep disorders:Melatonin is the hormone involved in the sleep – wake cycle[15]. It is easily synthesized and can be administered orally;therefore, it is considered as treatment for insomnia. Moreover, as production of hormone decreases with age It has been suggested that melatonin deficiency can be partly responsible for sleep disorders. Treating this age-related deficit would therefore appear to be a natural way of restoring sleep quality which is lost as patient age[16]. It is established now that melatonin is a

sleep-inducing substance. It increases duration of REM sleep therefore its role is considered in insomnia.

3. Mood disorders: Melatonin prepares one for sleep bringing energy levels down; thus, an increase in melatonin levels may lead to lower mood and depressive state. So, melatonin can be an etiological factor for depression. Seasonal affective disorder (SAD) which is seen in winter months when nights are long and more melatonin is being secreted. Melatonin worsens depression associated with SAD. If one must take melatonin for sleep disorders then he must take it with vitamin D to avoid depression associated with melatonin. When melatonin is high, vitamin D is low and vice versa. Increasing your exposure to sunlight in order to absorb more vitamin D may help improve your mood, counteracting the negative effects of melatonin[17,18].
4. Pineal gland as remnant of third eye:Pineal gland has a structure of pine cone. If one cuts this pine cone in to two halves, then it appears that it has structure similar to human eye. It consists of rod and cone structures as in retina. Similar pigments that are present in eyes are also traced here. Further, Pineal glands are light sensitive, thus making them very similar to eyes and hence, the name 'Third Eye' is somewhat justified. In 17th century, Rene Descartes (Father of modern Philosophy) named pineal gland as 'seat of soul'[19]. According to Hindu mythology, Pineal gland is also called as ajnachakra awakening of whose is related to awakening of 'third eye'. Mystic and esoteric spiritual traditions suggest it serves as a metaphysical connection between the physical and spiritual worlds[20].

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