The University of Burdwan
Three year UG course in Zoology under CBCS
DSE-4 (Endocrinology)

Pineal Gland

STRUCTUTE, SECRETION AND ITS FUNCTION IN BIOLOGICAL RHYTHM AND REPRODUCTION

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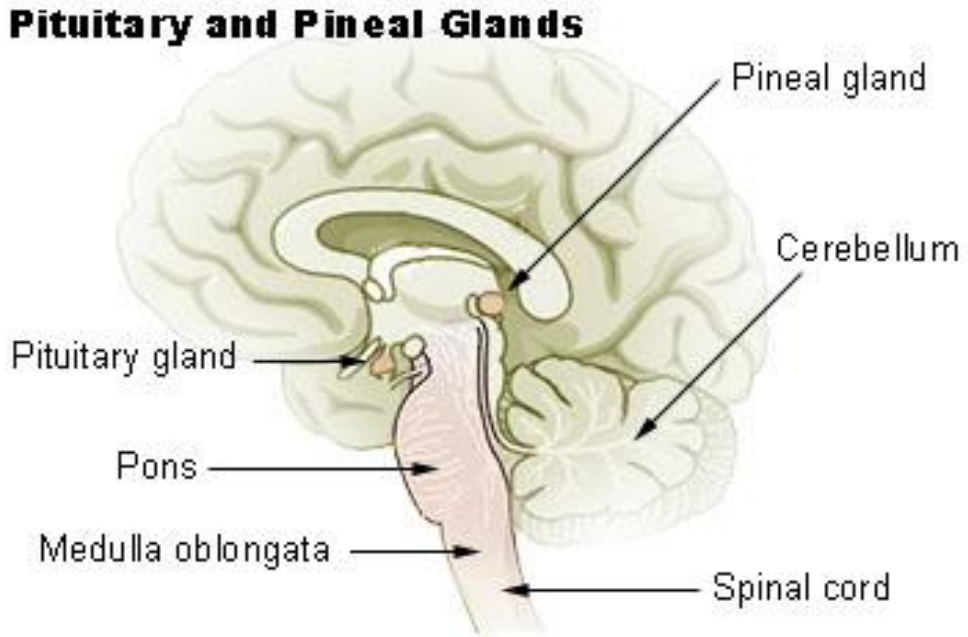
Pineal Gland

- The pineal gland or epiphysis or pineal body is a small pea-shaped or pine cone shaped (hence the name *pineal*) unpaired structure (**seat of the soul**), located deep inside the brain, between the two hemispheres.
- It plays a crucial role in regulating circadian rhythms through the secretion of **melatonin**.
- In lower vertebrates (e.g., fish, amphibians), it functions as a photoreceptive organ (**third eye**).
- In mammals, it has evolved into a neuroendocrine transducer, converting photoperiodic information into hormonal signals.
- It is a “windows on the circulation” or circumventricular organ (CVO) that serve as a conduit of peripheral cues into key neuronal cell groups that maintain homeostasis.

Images are from Anatomography maintained by Life Science Databases(LSDB)

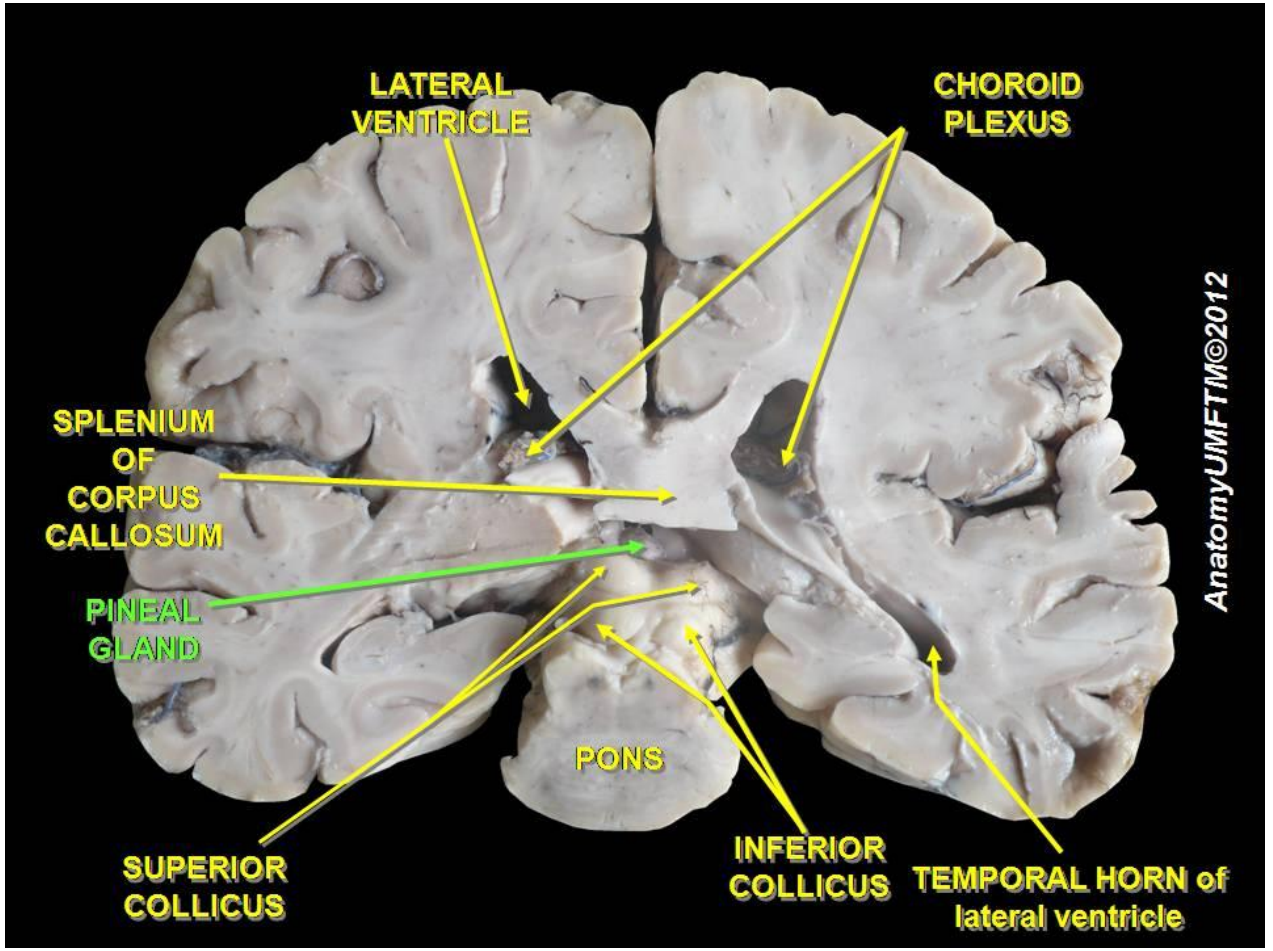


Location of the Pineal Gland

- The pineal gland, a small endocrine structure in the brain, occupies a central position within the cranial cavity.
- It is situated **between the left and right hemispheres**, approximately resembling the **size of a grain of rice (5-8 mm)**.
- This gland is unique as it is the only midline brain component that is **unpaired**, emphasizing its singular role in the central nervous system.

Location of the Pineal Gland

- Anatomically, the pineal gland is positioned in a region known as the **epithalamus**, which is part of the **diencephalon**.
- This strategic location places it **behind the third ventricle**, contributing to its central placement within the brain's architecture.
- The pineal gland is attached to the rest of the brain by the **pineal stalk**.

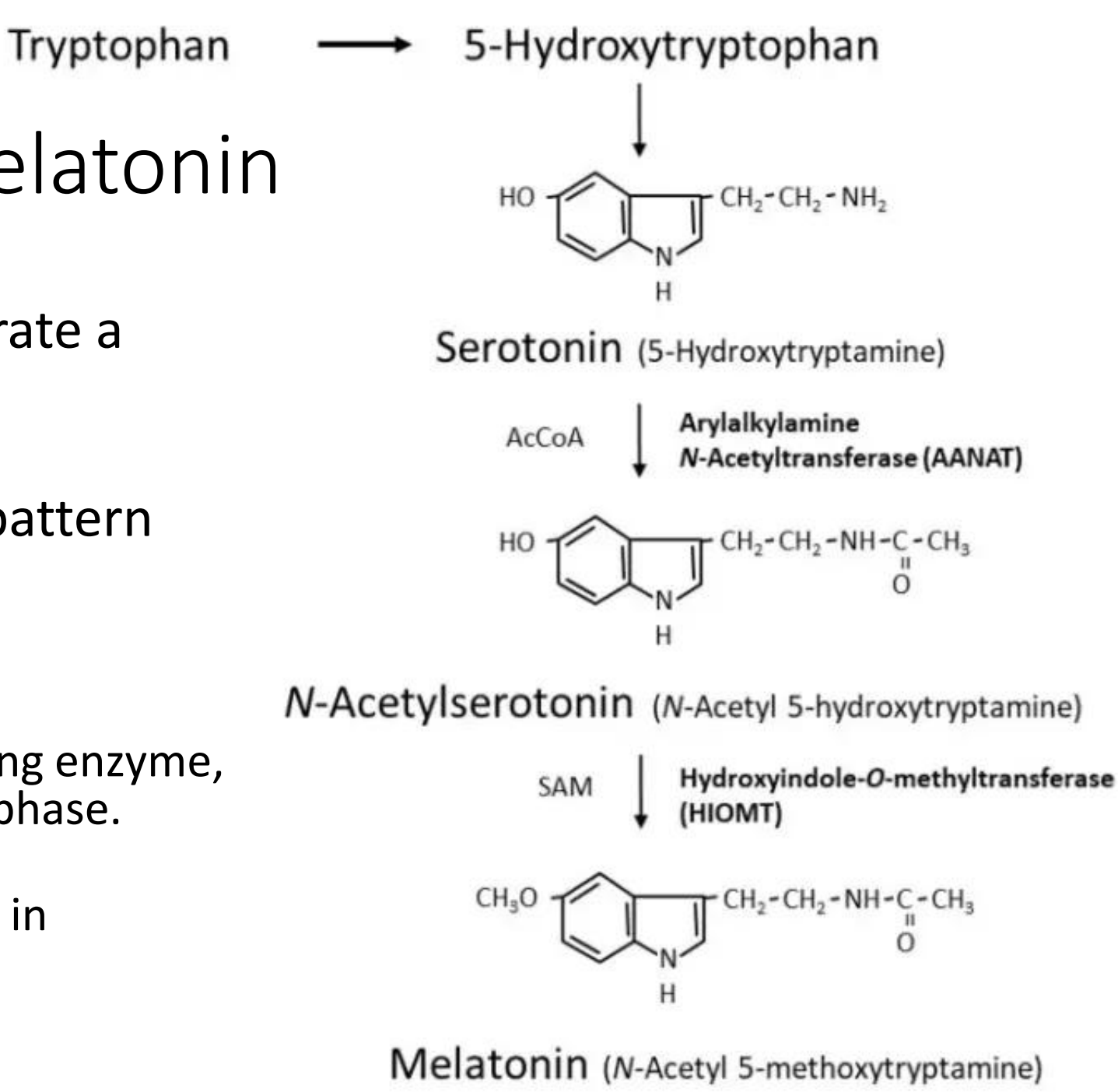


Structure of Pineal Gland

- Shape and size: Pinecone shaped (5-8 mm)
- Weight: 100-150 mg
- Attached to the other portion of the brain via Pineal stalk.
- Covered by a **pia mater capsule**
- Unlike most of the mammalian brain, the pineal gland is not isolated from the body by the blood–brain barrier system
- It has profuse blood flow, second only to the kidney, supplied from the choroidal branches of the posterior cerebral artery.
- Innervated by **postganglionic sympathetic fibres** from the **superior cervical ganglion (formed by C1-C4).**
- **Cell types:**
  - **Pinealocyte:**
    - Principal secretory cells (comprising 95% of the cells)
      - Large, irregular nuclei with prominent nucleoli
      - Possess long cytoplasmic processes terminating near capillaries
      - Synthesise and secrete melatonin
  - **Glial cells**
    - Provide structural and metabolic support
    - More numerous in aged glands
  - **Perivascular phagocyte**
    - Reside near the blood vessels, acts as antigen presenting cells.
  - **Pineal neurons**
    - In higher vertebrates neurons are usually located in the pineal gland. However, this is not the case in rodents.
  - Peptidergic neuron-like cells
    - In some species, neuronal-like peptidergic cells are present.
    - These cells might have a paracrine regulatory function.
- **Corpora Arenacea (Brain Sand):** Calcified structure commonly found in the pineal body, increases with age.

Pineal secretion: Melatonin

- Pinealocyte produce and secrate a Serotonin derived hormone **melatonin.**
- **Melatonin** modulates sleep pattern following the diurnal cycle.
- Key Enzymes Involved:
  - **AANAT (Arylalkylamine N-acetyltransferase):** Rate-limiting enzyme, active mainly during the dark phase.
  - **HIOMT (Hydroxyindole-O-methyltransferase):** Final step in melatonin synthesis.



Melatonin cycle and circadian rythm

- Norepinephrine (NE) acts as a primary neurotransmitter influencing melatonin synthesis. It primarily activates β-1 adrenergic receptors and, to some extent, α adrenergic receptors, enhancing AA-NAT activity.
- NE level increased during night (scrotophase), resulted in enhanced melatonin production.
- During light exposure (photophase), NE level decrease and also light triggers proteasomal proteolysis of melatoinin, resulted in the rapid decline in melatonin level.
- Melatonin levels peak at night (10 PM to 2 AM) and drop during daylight.

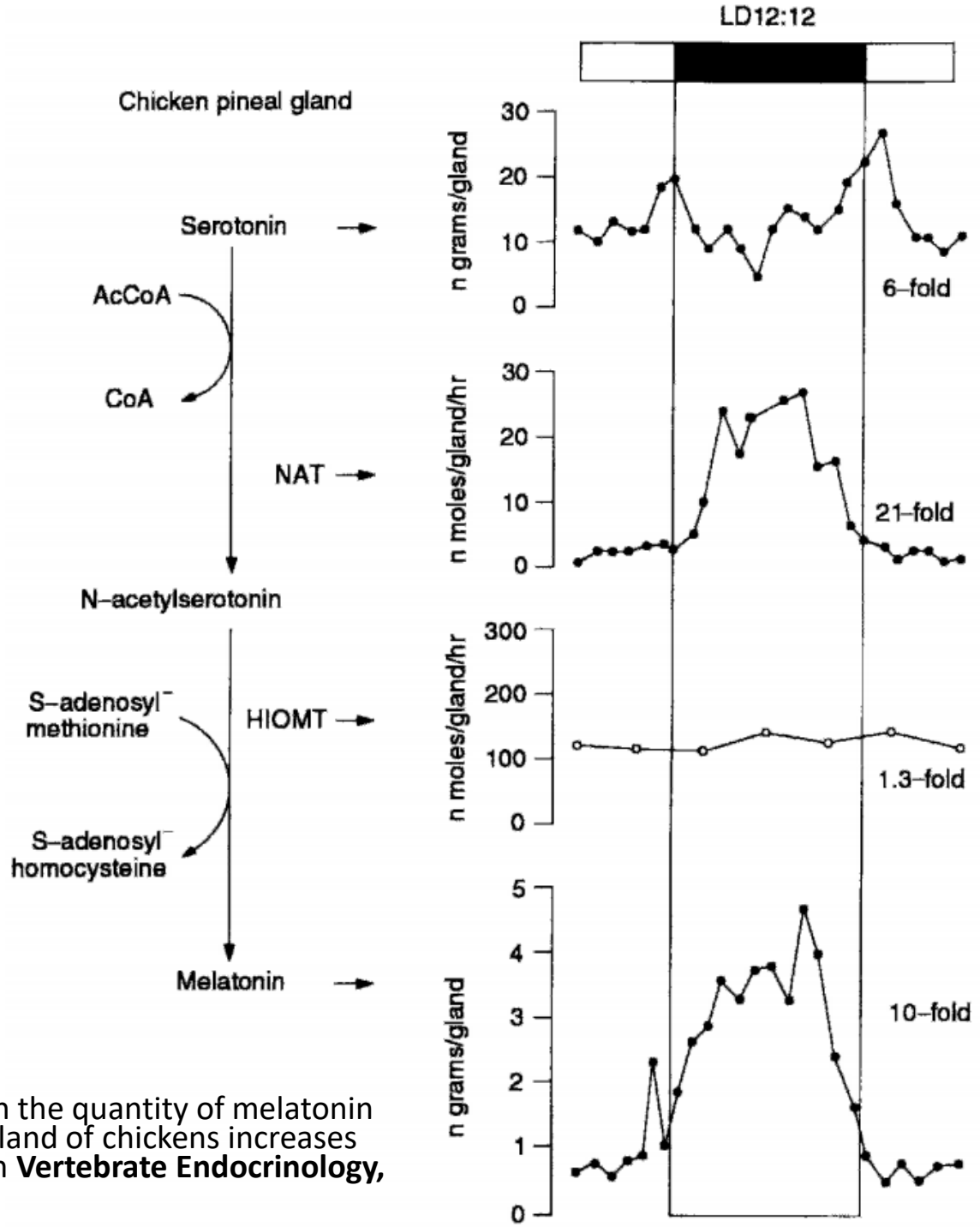


Figure: Serotonin and melatonin levels related to photoperiod and activity. Both the quantity of melatonin and activity of the rate-limiting enzyme N-acetyl transferase (NAT) in the pineal gland of chickens increases during the photophase. Similar observations have been made in mammals. (From **Vertebrate Endocrinology,** Fourth Edn., David O Norris)

Photoregulation of Melatonin

- Light sensitive nerve cells in the retina detect light and send this signal to the suprachiasmatic nucleus (SCN), synchronizing the SCN to the day-night cycle. Nerve fibers then relay the daylight information from the SCN to the paraventricular nuclei (PVN), then to the spinal cord and via the sympathetic system to superior cervical ganglia (SCG), and from there into the pineal gland.
- This pathway vis SCN is called **Retino-hypothalamic pathway**

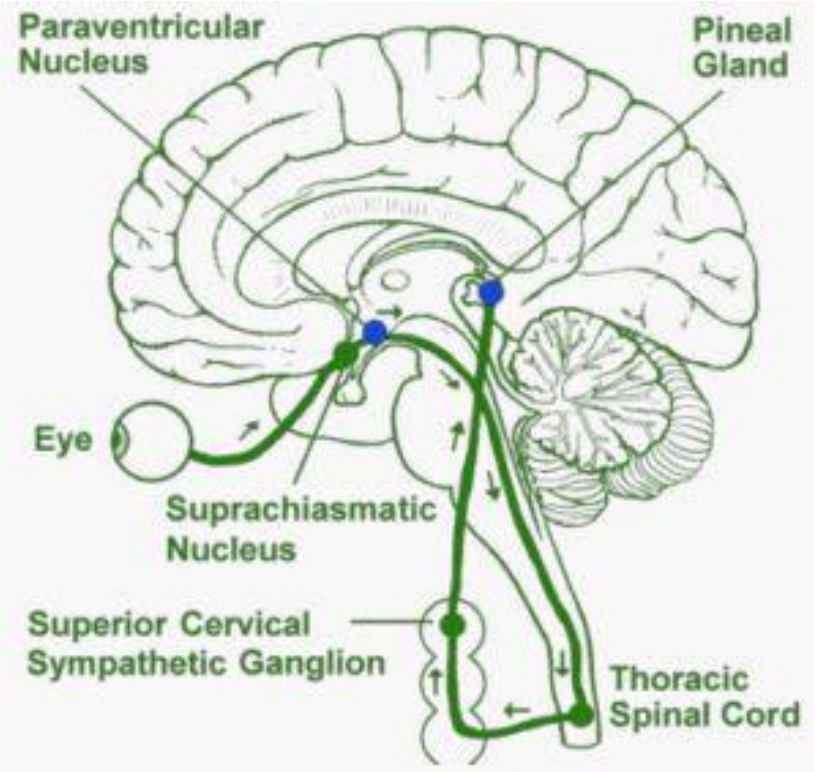
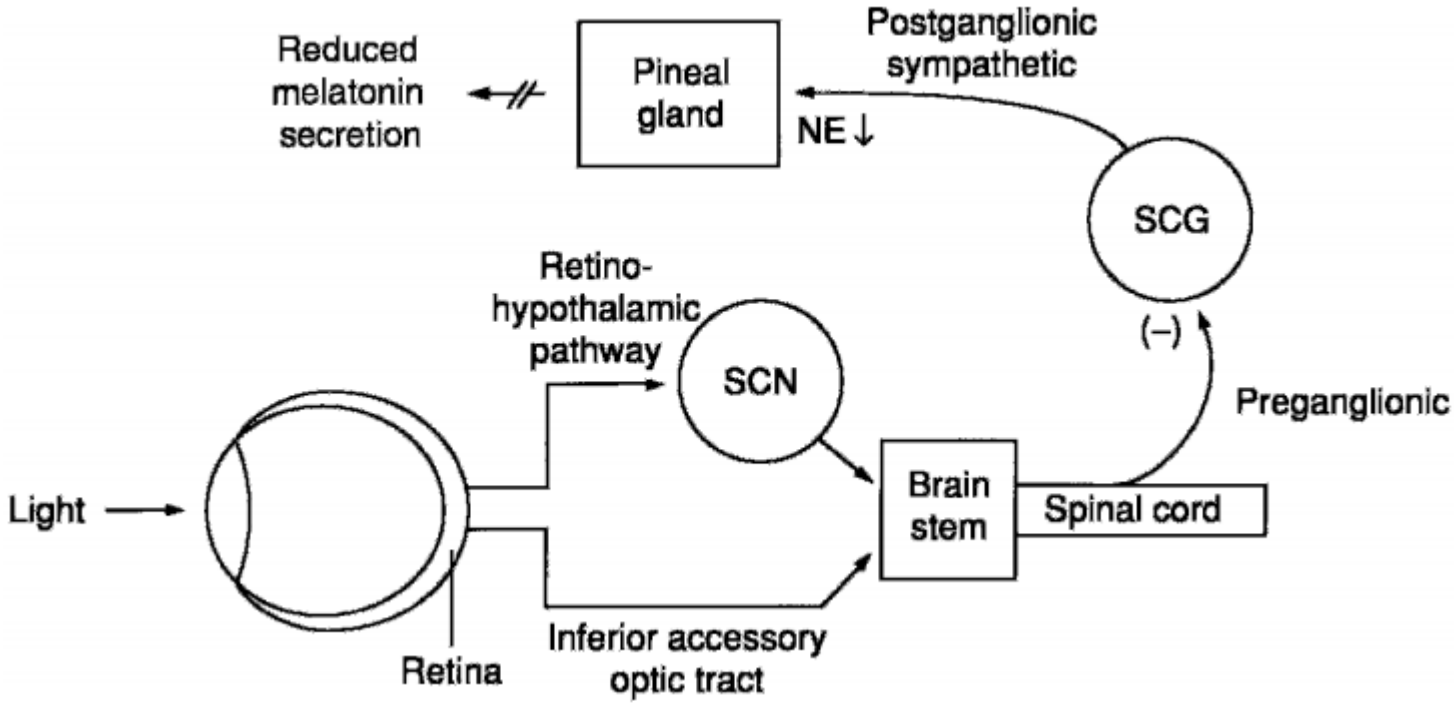


Figure: Regulation of pineal secretion by light. Light received by the retina inhibits pineal secretion via two central mechanisms (From **Vertebrate Endocrinology,** Fourth Edn., David O Norris)

Photoregulation of Melatonin

- Lesions in the **retinohypothalamic pathway or the SCN** do not necessarily abolish pineal secretory rhythms and led to the discovery of a second pathway between the retina and the brain stem that travels via the **inferior accessory optic tract**.



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Photoregulation of Melatonin

- Postganglionic fibers release NE.
- NE increase level of cAMP in the pinealocytes →cAMP increase the activity of AANAT → causes secretion of melatonin.
- NE secreting cells also secretes neuropeptide Y (NPY), that modulates responsiveness of pineal cells to NE.
- Light shining on the retina reduces NE input to the pineal, which resulted in reduction of cAMP level, reduced AANAT activity and reduced melatonin secretion.

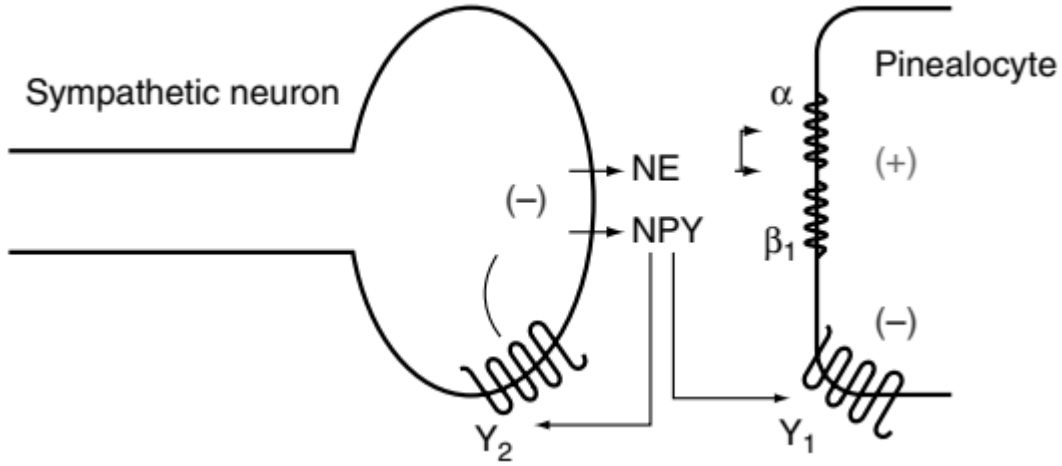

Figure: Neuropeptide Y (NPY) and its interactions with norepinephrine (NE). Activation of the release of melatonin is accomplished by NE secreted by sympathetic postgangionic neurons from the superior cervical ganglion. NPY acts as a local inhibitor to shut off the response to NE and also prevent additional NE release. Adrenergic receptors: α, β1. NPY receptors: Y1 Y2. (From **Vertebrate Endocrinology,** Fourth Edn., David O Norris)

Summary: Functions of melatonin to regulate biological rhythm

- Secretion of melatonin by the pineal gland is promoted by photoreception by retina.
- Dark condition increases melatonin.
- Melatonin promotes the onset of sleep by lowering core body temperature and reducing alertness.
- By sensing light-dark condition, pineal maintain biological rhythm.
- Melatonin is used therapeutically to manage jet lag, shift work disorders, and circadian rhythm sleep disorders.
- Disruption of melatonin rhythm linked to insomnia, depression, and metabolic dysfunction.

Melatonin and reproduction

Effect on Gonadal Function

- Melatonin influences **hypothalamic-pituitary-gonadal (HPG) axis**.
- Regulates secretion of **gonadotrophin-releasing hormone (GnRH)**.
- High melatonin levels → **inhibition** of GnRH → reduced **Follicle Stimulating hormone (FSH)** and **Luteinizing hormone (LH)** levels → suppressed gonadal activity.

Melatonin and reproduction

Photoperiodic Regulation and Seasonal Breeding

- The pineal gland, through melatonin secretion, plays a pivotal role in **seasonal reproductive rhythms** in animals.
- In **long-day breeders** (e.g., hamsters), increased melatonin during long nights suppresses reproduction.
- In **short-day breeders** (e.g., sheep), melatonin stimulates reproductive activity during shorter days.
- Pinealectomy (removal of the pineal gland) alters or abolishes these seasonal reproductive cycles, confirming melatonin's regulatory role.

Melatonin and reproduction

Non-seasonal breeder

- In non-seasonal breeder like rat and human melatonin still have effect on gonadal activities and puberty.
- Melatonin levels are high in childhood and decline before puberty, possibly removing inhibitory signals and enabling GnRH pulsatility and pubertal onset.
- Delayed puberty is often associated with elevated nocturnal melatonin.
- In precocious puberty, melatonin levels are typically lower than in age-matched prepubertal children.
- Melatonin receptor also found in gonad, stimulate steroidogenesis, suggests direct effect of melatonin on gonad.
- Mixed evidence on correlation between melatonin and menstrual phases.
- Disruptions in melatonin rhythms (e.g., in amenorrhoea, anorexia) are associated with menstrual irregularities.
- Phototherapy and melatonin administration have shown promise in restoring cycle regularity in some disorders.

Melatonin and reproduction

Table I. Melatonin and reproduction of seasonal breeders, non-seasonal breeders and humans

Species	Breeding season	Influence of melatonin on HPO axis	Effects of long-term melatonin administration	Mechanism of action of melatonin
Hamster (long day breeder)	spring–summer	inhibitory	delayed puberty Gonadal involution	GnRH inhibition
Sheep (short day breeder)	autumn–winter	stimulatory	enhanced reproductive activity increased pulsatile LHRH and LH	GnRH stimulation
Rat (non-seasonal breeder)	—	inhibitory	delayed puberty absence of the pro-oestrous LH surge Anovulation	GnRH inhibition GnRH-induced LH release inhibition
Human	—	inhibitory	decreased plasma LH (with absence of the mid-cycle surge), oestradiol & progesterone Anovulation	GnRH inhibition[a] GnRH-induced LH inhibition[a] Direct action on gonads

GnRH = gonadotrophin-releasing hormone; LHRH = luteinizing hormone-releasing hormone; LH = luteinizing hormone; HPO = hypothalamic–pituitary–ovarian.
[a]GnRH inhibition is more likely than GnRH-induced LH inhibition.

Exercise

- Write the structure of Pineal Gland (4)
- Which hormone is mainly secreted by Pineal Gland (5)
- Write the role of melatonin in regulating circadian rhythm. (5)
- Write the role of melatonin on reproduction. (5)
- What is the key enzyme in melatonin synthesis? (1)
- Which neurotransmitter affect melatonin synthesis? (1)
- How does light signal affect melatonin synthesis? (5)