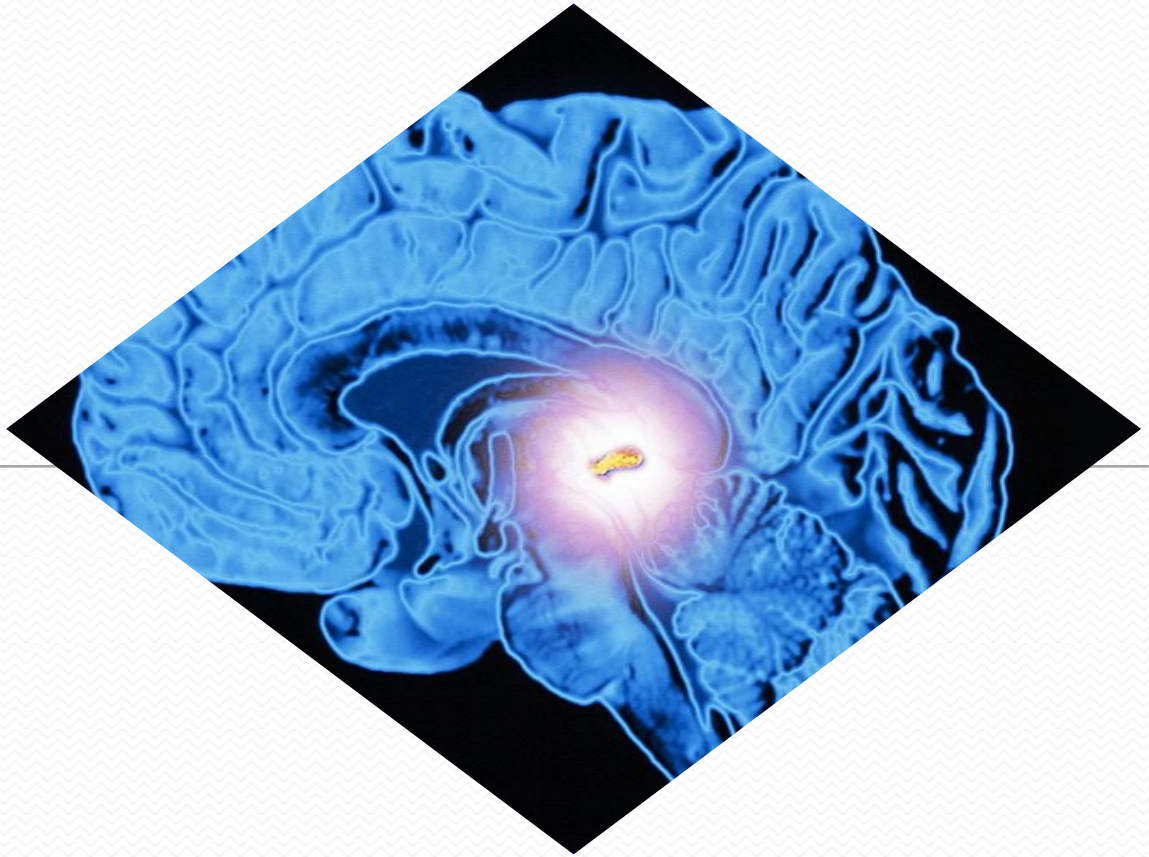
# Pineal Gland

By Dr. Subarna Ghosh



# What is the Pineal Gland?

- **Pineal gland**, also called **conarium, epiphysis cerebri, pineal organ,** or **pineal body.**

- It is an endocrine gland found in vertebrates that is the source of melatonin, a hormone derived from tryptophan.

- Melatonin plays a central role in the regulation of circadian rhythm (the roughly 24-hour cycle of biological activities associated with natural periods of light and darkness).

- The pineal gland has long been an enigmatic structure. Even in the early 21st century, when sophisticated molecular techniques were available for biological study, fundamental features of the gland—including the extent of the effects of its principal hormone, melatonin—remained incompletely understood.

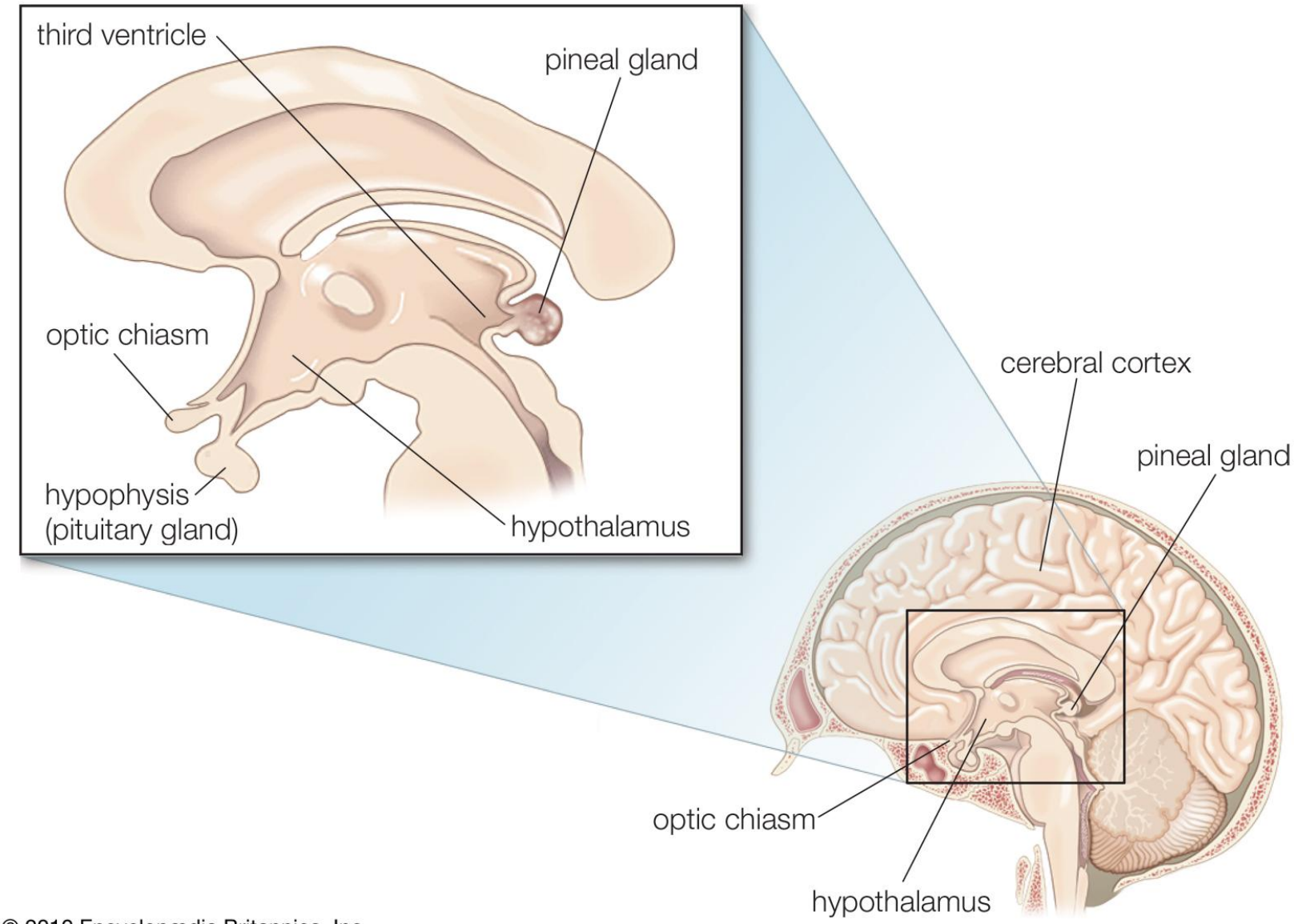
# Anatomy of Pineal Gland

- The pineal gland develops from the roof of the diencephalon, a section of the brain, and is located behind the third cerebral ventricle in the brain midline (between the two cerebral hemispheres).

- Its name is derived from its shape, which is similar to that of a pinecone (Latin *pinea*).

- In adult humans it is about 0.8 cm (0.3 inch) long and weighs approximately 0.1 gram (0.004 ounce).

- The pineal gland has a rich supply of adrenergic nerves (neurons sensitive to the adrenal hormone epinephrine) that greatly influence its function.



# Anatomy of Pineal Gland?

- Microscopically, the gland is composed of pinealocytes (rather typical endocrine cells except for extensions that mingle with those of adjacent cells) and supporting cells that are similar to the astrocytes of the brain.

- In adults, small deposits of calcium often make the pineal body visible on X-rays. (The pineal gland eventually becomes more or less calcified in most people.)

- In some lower vertebrates the gland has a well-developed eyelike structure. In others, though not organized as an eye, it functions as a light receptor.

# Pineal Hormones

✓Both melatonin and its precursor, serotonin, which are derived chemically from the alkaloid substance tryptamine, are synthesized in the pineal gland.

✓Along with other brain sites, the pineal gland may also produce neurosteroids. Dimethyltryptamine (DMT), a hallucinogenic compound present in the Amazonian botanical drink ayahuasca, is chemically similar to melatonin and serotonin and is considered to be a trace substance in human blood and urine.

✓Although alleged to be produced by the pineal gland, DMT has not been consistently detected in human pineal microdialysates (purified pineal extracts), and proof of its regulated biosynthesis in the mammalian pineal gland is lacking.

✓ Thus, though the conclusion by 17th-century French philosopher René Descartes that the pineal gland is the seat of the soul has endured as a historical curiosity, there is no evidence to support the notion that secretions from the pineal have a major role in cognition.

# Melatonin Synthesis

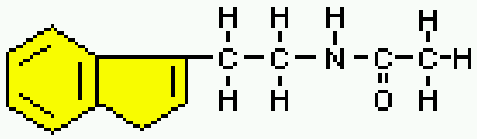
- ✓In addition to the pineal gland, melatonin is also synthesized in the vertebrate retina, where it transduces information about environmental light through local receptors designated MT1 and MT2, and in certain other tissues, such as the gastrointestinal tract and the skin.

- ✓In generally rate-limiting step of melatonin biosynthesis, an enzyme called serotonin N-acetyltransferase (AANAT) catalyzes the conversion of serotonin to N-acetylserotonin.

- ✓Subsequently that compound is catalyzed to melatonin by acetylserotonin *O*-methyltransferase (ASMT).

# Melatonin Synthesis

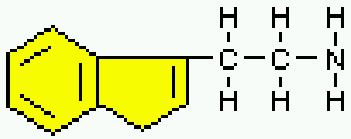
**N-acetylserotonin**



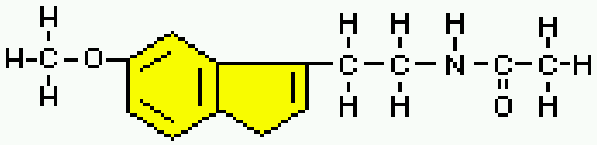
serotonin N-acetyltransferase

acetylserotonin *O*-methyltransferase

**Serotonin**



**Melatonin**



# Melatonin

✓The rise in circulating melatonin concentrations that occurs and is maintained after sundown and with darkness coincides with the activation of AANAT during dark periods.

✓ Melatonin concentrations also are higher in the cerebrospinal fluid (CSF) of the third ventricle of the brain than in the CSF of the fourth ventricle or in the blood.

✓ That suggests that melatonin is also secreted directly into the CSF, where it may have direct and perhaps more-sustained effects on target areas of the central nervous system.

✓Synthesis and secretion of melatonin is dramatically affected by light exposure to the eyes. The fundamental pattern observed is that serum concentrations of melatonin are low during the daylight hours, and increase to a peak during the dark.

# Regulation of Melatonin Secretion

✓In some species pineal cells are photosensitive.

✓In humans and higher mammals a “photoendocrine system”—made up of the retina, the suprachiasmatic nucleus of the hypothalamus, and noradrenergic sympathetic fibres (neurons responsive to the neurotransmitter norepinephrine) terminating in the pineal—provides light and circadian information that regulates pineal melatonin secretion.

✓ In contrast to many other endocrine hormones, human melatonin concentrations are highly variable, and serum melatonin levels decline markedly during childhood, as there is little or no growth of the pineal gland after about one year of age.

# Melatonin Receptors in Mammals

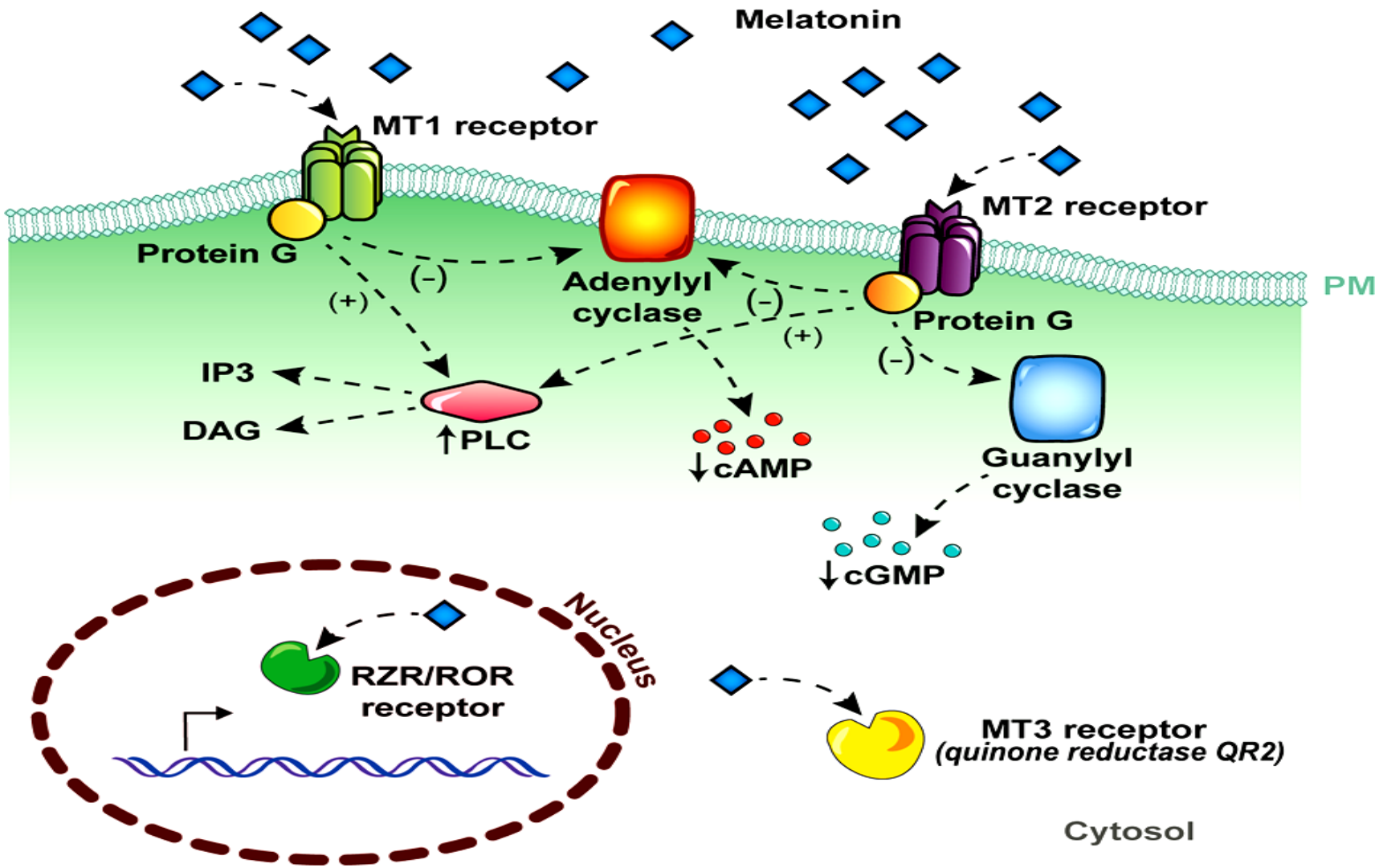
✓Two melatonin receptors have been identified from mammals that are differentially expressed in different tissues and probably participate in implementing differing biologic effects.

✓These are G protein-coupled cell surface receptors. The highest density of receptors has been found in the suprachiasmatic nucleus of the hypothalamus, the anterior pituitary (predominantly pars tuberalis) and the retina.

✓ Receptors are also found in several other areas of the brain.

✓Melatonin is synthesized not only in the pineal gland, but in a broad range of other tissues. It is also present in all microorganisms, animals and plants, consumption of which is also an additional source of melatonin.

# Melatonin Receptors in Mammals



# Melatonin in the Sleep-Wake Cycle

- It appears that the function of melatonin is to mediate dark signals and provide night information, a “hormone of darkness,” rather than be the hormone of sleep.

- It has also been thought to be an “endogenous synchronizer” that stabilizes and reinforces various circadian rhythms in the body.

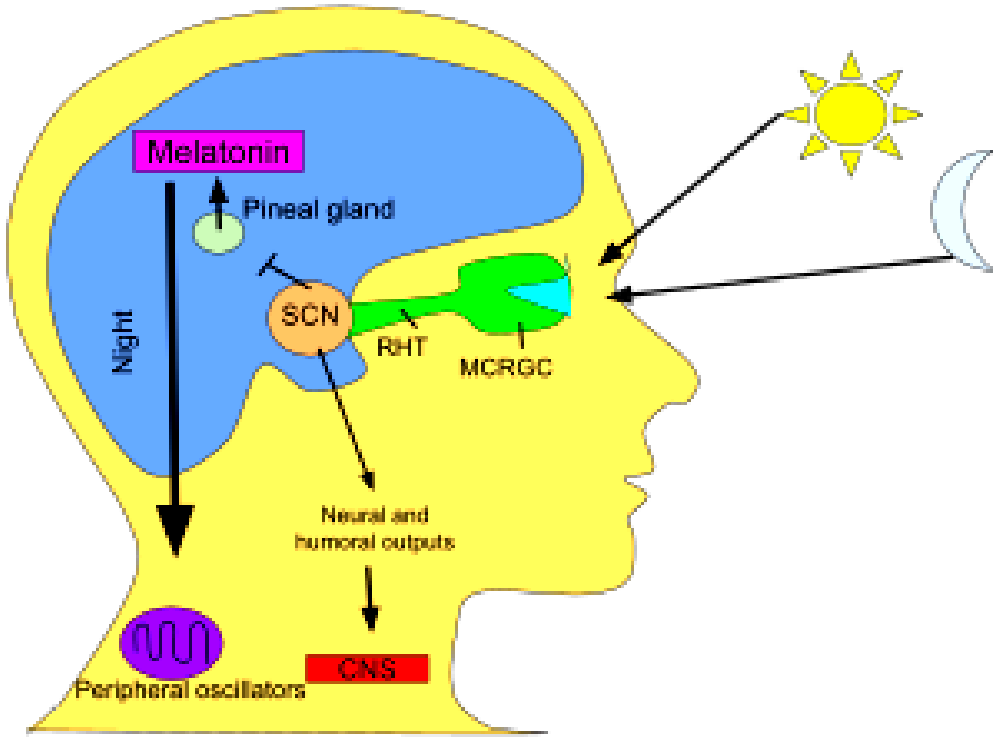
- The daily sleep-wake cycle is influenced by 2 factors: process C (circadian), an endogenous “clock” that drives the rhythm of the sleep-wake cycle; and process S (sleep), a homeostatic “sleep propensity” that determines the recent amount of sleep and wakefulness accumulated.

# Melatonin in the Sleep-Wake Cycle

- The SCN interacts with both processes, and it is where the main component of process C (cercadian) is located.

- Excitatory signals from the SCN and subsequent melatonin suppression are thought to promote wakefulness during the day in response to light and the suppression of melatonin inhibition of the SCN.

- This inhibition is released in the dark phase and leads to melatonin synthesis/release with consequent sleep promotion.



# Melatonin and Sleep disorders

- Melatonin is probably not a major regulator of normal sleep patterns, but undoubtedly has some effect.

- One topic that has generated a large amount of interest is using melatonin alone, or in combination with phototherapy, to treat sleep disorders.

- There is some indication that melatonin levels are lower in elderly **insomniacs** relative to age matched non-insomniacs, and melatonin therapy in such cases appears modestly beneficial in correcting the problem.

- Another sleep disorder is seen in **shift workers**, who often find it difficult to adjust to working at night and sleeping during the day. The utility of melatonin therapy to aleviate this problem is equivocal and appears not to be as effective as phototherapy.

# Melatonin and Jet lag

- Still another condition involving disruption of circadian rhythms is **jet lag**. In this case, it has repeatedly been demonstrated that taking melatonin close to the target bedtime of the destination can alleviate symptoms; it has the greatest beneficial effect when jet lag is predicted to be worst (e.g. crossing many time zones).

- In various species, including humans, administration of melatonin has been shown to decrease motor activity, induce fatigue and lower body temperature, particularly at high doses. The effect on body temperature may play a significant role in melatonin's ability to entrain sleep-wake cycles, as in patients with jet lag.

# Pineal Physiology And Pathophysiology

- In humans both precocious puberty and delayed puberty have been associated with pineal tumours and cysts.

- However, the pathogenesis leading to those conditions is unclear, and both mechanical and hormonal factors may be involved.

- Positive relationships between melatonin secretion and some other hormones have been reported, though pure melatonin-secreting tumours have not been observed. Indeed, in contrast to other endocrine glands, such as the pituitary, adrenal, and thyroid, there are no well-defined pineal hormone-deficiency or hormone-excess syndromes.

# THANK YOU