Melatonin Action on Pineal Varies with Photoperiod

Abstract. *Administration of melatonin can prevent the diurnal rhythm of serotonin concentration characteristic of the pineal organ. Whether or not such a change is induced depends upon the point in the photoperiod when the hormone is injected. This observation indicates that the action of melatonin is affected by the photic environment of the recipient.*

A number of investigators have pointed out that, even now, assessment of the physiological role of the pineal organ is difficult. One reason may be that this gland appears to be periodically active and may be effective only when its active compounds (*1*), such as melatonin and 5-hydroxytryptophol, operate at a given time in the photoperiod. With this hypothesis in mind we have studied the effect of melatonin on the pineal organ in rats receiving carefully timed injections of this hormone at two particular point in the photoperiod.

Ninety-five young adult (initially 10 to 12 weeks old) female Sprague-Dawley rats were given daily subcutaneous injections of melatonin (50 μg in 0.2 ml oil), or the vehicle only, for 4 weeks (*2*). All animals were housed in rooms equipped with humidity and temperature controls and were exposed to 14 hours of light (*3*) (242 to 330 lumen/m^2 at cage level) followed by 10 hours of dark. As originally reported by Quay and later confirmed in this laboratory (*4, 5*), under these environmental conditions the pineal gland of the laboratory rat exhibits a diurnal rhythm of serotonin concentration. Its serotonin concentration reaches a maximum at the 8th hour of the light period, falls off rapidly with the onset of darkness, and reaches a minimum 4 hours later. Since the melatonin content of the pineal gland in the rat increases diurnally in the dark period and since the enzyme hydroxyindole-O-methyl transferase, necessary for the final step in the conversion of serotonin to melatonin, is suppressed by light, it appears that the serotonin rhythm reflects in an inverse fashion the production of melatonin (*6*).

We therefore injected melatonin at the 8th hour of the light period when little if any melatonin would normally be available to the rat, and during the 14th hour, just a few minutes before the onset of darkness when the rat's pineal seems to begin producing and releasing increased amounts of melatonin. At the end of the 28-day injection period the animals were killed, by a quick blow to the head, at any one of three specific points in the photoperiod. Their pineals were removed, individually extracted and, within 24 hours, they were assayed fluorometrically for serotonin by methods previously reported (see *5, 7*).

We found a well-defined serotonin rhythm in the oil-injected controls when their pineals were removed at the 8th hour of light or the 3rd hour of darkness and compared for serotonin content. Such a rhythm was not evident in rats receiving melatonin at the 8th hour of light although it was present and even appeared to be somewhat more marked in rats injected with melatonin as darkness fell (Table 1).

To check the possibility that melatonin given at the 8th hour of light was inducing a premature drop in serotonin which we were not detecting we killed 12 rats, given melatonin or oil daily at the 8th hour of light as previously described, three hours later, and analyzed their pineals for serotonin content. No drop in serotonin concentration was observed, an average of slightly more than 100 ng of serotonin per gland being found in both groups.

These results demonstrate that melatonin directly, or indirectly through the nervous system, shifts or blocks the usual serotonin rhythm of the pineal when the hormone is given at a specific time in the photoperiod; they indicate that other parameters affected by melatonin should be reexamined in animals receiving injections at different times in the photoperiod.

Table 1. Effect of timed injections of melatonin or oil on pineal serotonin concentration (nanograms per gland); S.E., standard error of the mean.

Removal of pineal		Treatment			
		Oil		Melatonin	
Hour	Cycle	Animals (No.)	Mean ± S.E.	Animals (No.)	Mean ± S.E.
		Animals injected 8th hour of light			
8	light	10	124 ± 15.6	13	103 ± 10.5
3	dark	14	65 ± 10.7	15	87 ± 11.0
			$P < .005$		$P < .4$
		Animals injected 14th hour of light			
8	light	8	107 ± 10.8	7	101 ± 9.1
3	dark	8	62 ± 9.7	8	36 ± 3.5
			$P < .025$		$P < .001$

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References and Notes

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Long-Lasting Hyperpolarization after Activity of Neurons in Leech Central Nervous System

Abstract. *After a train of impulses, the membrane potential of sensory neurons may be increased for several minutes by an electrogenic pump. During this hyperpolarization, the sensitivity of the membrane potential to external potassium ions is increased, so that physiologically occurring increases in potassium concentration could influence synaptic processes.*

In crustacean stretch receptors, snail neurons, and mammalian C-fibers, a train of action potentials is followed by an increase in membrane potential that lasts seconds or minutes (*1*). This after-hyperpolarization is due to an electrogenic pump, which extrudes the Na^+ that has entered the cell during activity. Our experiments show that a similar hyperpolarization occurs after activity