Light at Night, Circadian Rhythms, and Melatonin Production: Implications for Pediatrics

Russel J. Reiter
University of Texas Health Science Center
San Antonio, Texas
reiter@uthscsa.edu

Evolution has dictated biological rhythmicity and physiology influenced by the light/dark cycle.

The pineal gland is the source of the circadian blood melatonin rhythm.

N-acetyl-5-methoxytryptamine (melatonin)
The eyes are required for light inhibition of melatonin production and for adjusting circadian rhythms.

Classic photoreceptors (rods and cones) are not involved in regulation of circadian rhythms.

Light regulation of circadian rhythms involves a unique set of ganglion cells and melanopsin.

Blue-green wavelengths (peaking at 460-480 nm) are most inhibitory to the biological clock and melatonin levels.

Light regulation of the biological clock and pineal melatonin production.

1879, a critical year for melatonin and circadian rhythms.

The quantity of melatonin produced is proportional to the duration of darkness.

Light at night suppresses melatonin levels proportional to the brightness

Essentially every function in the body exhibits a 24 hour rhythm

Simulated jet lag, due to desynchronization of circadian rhythms, accelerates tumor growth

Growth rate of two tumor types after lesions of the SCN (- -), the biological clock

Severely altered (inverted) melatonin rhythm and major sleep disorders in individuals with Smith-Magenis syndrome


Filipski E & Delauney F, Cancer Res 2004; 64: 7879-85

Filipski E & Li XM, Cancer Causes Control, 2006; 17: 509-14
Simulated jet lag (or lesions of the SCN) eliminates the circadian melatonin rhythm

Plasma Melatonin (pg/ml)

1800 0800

Simulated jet lag (or lesions of the SCN) eliminates the circadian melatonin rhythm

Down regulation of Per2 accelerates cell growth and elevates Cyclin D and Cyclin E levels in murine mammary tumor cells in vitro


Environmental factors are among the major determinants of epigenetic changes related to carcinogenesis

Fraga MF et al, Ann NY Acad Sci 2007; 1100: 60-74

Elevated SIRT1 also deacetylates FOXOs which upregulate genes for DNA repair and detoxifying enzyme activities while downregulating genes for cell cycle arrest and apoptosis

Carter ME & Brunet A, Curr Biol 2008; 17: R113-4
Telomeres are ribonucleoprotein structures that protect chromosomes but shorten with each cell division in normal cells; in cancer cells they are maintained.

**Melatonin inhibits human MCF-7 cancer cell growth**


**Melatonin inhibits tumor growth and tumor metastases**


**Melatonin reduces telomerase activity in MCF-7 cancer cells (TRAP assay)**


Aspects of the immune system that are stimulated by melatonin that may contribute to its oncostatic effects

Srinivasan V et al, Integrat Cancer Ther 2008; 7: 189-203

Light at night is classified as a Group 2A carcinogen possibly due to (a) melatonin suppression (b) chronodisruption (c) sleep deprivation (d) more likely a combination of all of the above.
Melatonin in the drinking water of middle-aged rats reduces insulin and leptin levels

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 9)</th>
<th>Melatonin (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat mass (g)</td>
<td>76.7 ± 5.7</td>
<td>73.3 ± 5.8</td>
</tr>
<tr>
<td>Fat mass (% of carcass)</td>
<td>14.8 ± 0.9</td>
<td>15.4 ± 1.0</td>
</tr>
<tr>
<td>Lean mass (g)</td>
<td>428 ± 9</td>
<td>391 ± 7</td>
</tr>
<tr>
<td>Lean mass (% of carcass)</td>
<td>63 ± 1</td>
<td>85 ± 1</td>
</tr>
<tr>
<td>Visceral fat mass (g)</td>
<td>18.2 ± 1.3</td>
<td>14.5 ± 1.1</td>
</tr>
<tr>
<td>% of total fat mass (%)</td>
<td>23.8 ± 0.7</td>
<td>19.9 ± 1.0</td>
</tr>
<tr>
<td>% of carcass</td>
<td>3.5 ± 0.2</td>
<td>3.0 ± 0.2</td>
</tr>
<tr>
<td>Peripheral fat mass (g)</td>
<td>56.5 ± 4.5</td>
<td>58.8 ± 4.5</td>
</tr>
<tr>
<td>% of total fat mass (%)</td>
<td>76.2 ± 0.7</td>
<td>80.1 ± 0.9</td>
</tr>
<tr>
<td>% of carcass</td>
<td>11.3 ± 0.7</td>
<td>12.4 ± 0.9</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>179.3 ± 5.8</td>
<td>171.9 ± 6.5</td>
</tr>
<tr>
<td>Insulin (ng/ml)</td>
<td>2.7 ± 0.2</td>
<td>2.0 ± 0.2</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>5.8 ± 0.5</td>
<td>3.9 ± 0.6</td>
</tr>
</tbody>
</table>

Wolden-Hanson T et al, Endocrinology 2000; 141: 487-97