Circannual concentrations of melatonin, gonadotrophins, prolactin and gonadal steroids in males in a geographical area with a large annual variation in daylight

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Abstract. This study was aimed at elucidating the possible effects of a large annual variation in photoperiodicity on the secretory activities of the pineal gland, pituitary and testes. Serum daytime melatonin, FSH, LH, prolactin (Prl), testosterone and oestradiol concentrations were determined monthly over a year in 24 healthy young adult men (except for melatonin which was analysed only in 11 subjects) in northern Finland, where the day length is 22 h in mid-summer and 3.5 h in mid-winter. Serum daytime melatonin levels showed two annual peak values, in December and May, and a nadir was observed in August. The absolute values of the other hormones measured did not show significant month to month variation over the observation period. When hormone levels were calculated as percentages of the individual annual means, several significant differences were found between monthly levels. The melatonin peak in May (133 ± 20%, SE, of the annual mean) was associated with significant increases in LH (110 ± 4%) and FSH (107 ± 3%). Prl levels (115 ± 9%) reached a maximum in January. The nadirs of melatonin and the pituitary hormones measured were seen in August. Oestradiol showed the highest values in April-June, but no significant variation was found in serum testosterone levels. Positive correlations were observed between FSH and LH (r = 0.41, P < 0.01), and Prl and LH (r = 0.26, P < 0.01), whereas Prl and testosterone (r = -0.17, P < 0.01) were inversely correlated.

This study indicates circannual rhythmicity of peripheral serum daytime melatonin, gonadotrophin, Prl and oestradiol levels, but this variation was not related to extremes in daylight and therefore seasonal factors other than light may regulate this circannual variation.

The synthesis of melatonin in the pineal gland is known, at least in animals, to be dependent on exposure to light, and a clear daily rhythm in melatonin secretion with peak values during the night has been reported (Vaughan et al. 1978). An annual variation with peaks in January and July has also been documented (Arendt et al. 1979).

The changes in melatonin secretion in animals are associated with circannual rhythmicity in gonadal function, possibly due to the melatonin-induced inhibition of gonadotrophin secretion (see, e.g. Mas et al. 1979), but a direct action on the gonads cannot be ruled out (Reppert & Klein 1980). In man the regulatory role of melatonin in reproductive function is still poorly understood.

Data concerning annual variation of pituitary gonadal hormones in man are scarce. Circannual rhythms in LH, FSH and testosterone secretion have been reported in young men (Reinberg et al. 1978; Smals et al. 1976) and the LH results were recently confirmed by Touitou et al. (1983). In
contrast, no seasonal variation was found in serum prolactin (Prl) (Gala et al. 1977; Reinberg et al. 1978; Djursing et al. 1981).

The previous studies (above) on circannual variation in the pituitary-gonadal axis were performed in central Europe, and the seasonal variations observed were considered to be due, at least partly, to variations in the length of daylight. The rationale of the present study was therefore to investigate whether a larger annual variation in photoperiodicity could reveal more pronounced circannual variations in the functions of the pineal gland, pituitary and testes. The present report is an extension of our previous work on circannual levels of testosterone in young men (Huhtaniemi et al. 1982).

Materials and Methods

This study was performed in the city of Oulu in northern Finland (65°N and 25° 30' E of Greenwich). In mid-June the day length is 22 h, and in mid-December 3.5 h.

Twenty-four normal healthy men (laboratory personnel and medical students) participated in the study. The mean age of the subjects at the beginning of the experiment was 24.9 years (range 21–41 years). A peripheral vein blood sample was taken on the second Tuesday of each month between 10–12 a.m. The sampling was continued for 15 consecutive months. The sera were separated by centrifugation and stored at −20°C until analyzed. The subjects were asked to abstain from alcohol and excessive physical exercise for a day before blood sampling.

Serum testosterone was measured by radioimmunoassay as previously described (Hammond et al. 1977). The intra-assay coefficient of variation (CV) was below 5%, and the inter-assay CV 6.2%. Oestradiol concentrations were determined by a radioimmunoassay kit provided by Farnos Diagnostica (Oulunsalo, Finland). The intra-assay CV was found to be 7% and the inter-assay CV 7.7%. Serum FSH and LH levels were measured using CEA-IRE-SORIN (GIS) kits (Institut National des Radioelements, Fleurus, Belgium). The FSH and LH results were standardized against LER 907, MRC 69/104 (FSH) and 68/40 (LH). The inter-assay CV:s for FSH and LH were 5.5 and 6.5%, respectively. Serum concentrations of Prl were determined by using a commercial radioimmunoassay kit provided by Kabi Diagnostica (Stockholm, Sweden), following the instructions of the manufacturer. The standard was calibrated against the NIH reference preparation VLS No. 3. The inter-assay CV was 10.6%.

Serum melatonin concentrations were analyzed in 11 of the subjects by using a recently developed radioimmunoassay (Vakkuri et al. 1984). [125I]melatonin was used as tracer, and the antiserum was raised in rabbits by immunization with a bovine thyroglobulin conjugate of 

<table>
<thead>
<tr>
<th>Month</th>
<th>Testosterone nmol/l (n = 24)</th>
<th>Oestradiol nmol/l (n = 24)</th>
<th>LH IU/l (n = 24)</th>
<th>FSH IU/l (n = 24)</th>
<th>Prl µg/l (n = 24)</th>
<th>Melatonin pmol/l (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>October</td>
<td>12.4 ± 1.0</td>
<td>0.08 ± 0.01</td>
<td>9.3 ± 0.6</td>
<td>5.6 ± 0.7</td>
<td>8.5 ± 1.1</td>
<td>34.9 ± 4.7</td>
</tr>
<tr>
<td>November</td>
<td>12.5 ± 1.1</td>
<td>0.09 ± 0.01</td>
<td>9.1 ± 0.8</td>
<td>5.2 ± 0.6</td>
<td>6.6 ± 0.4</td>
<td>29.7 ± 3.5</td>
</tr>
<tr>
<td>December</td>
<td>12.7 ± 1.2</td>
<td>0.11 ± 0.02</td>
<td>9.3 ± 0.8</td>
<td>5.2 ± 0.6</td>
<td>7.7 ± 1.0</td>
<td>37.1 ± 6.9B</td>
</tr>
<tr>
<td>January</td>
<td>11.7 ± 1.1</td>
<td>0.08 ± 0.01</td>
<td>8.4 ± 0.7</td>
<td>5.1 ± 0.5</td>
<td>9.1 ± 1.4</td>
<td>28.4 ± 2.6</td>
</tr>
<tr>
<td>February</td>
<td>11.7 ± 1.1</td>
<td>0.10 ± 0.02</td>
<td>9.9 ± 0.7</td>
<td>5.4 ± 0.5</td>
<td>7.1 ± 0.5</td>
<td>27.2 ± 4.3</td>
</tr>
<tr>
<td>March</td>
<td>11.3 ± 0.9</td>
<td>0.09 ± 0.01</td>
<td>9.1 ± 0.6</td>
<td>5.4 ± 0.5</td>
<td>6.7 ± 0.7</td>
<td>23.7 ± 2.1a</td>
</tr>
<tr>
<td>April</td>
<td>12.5 ± 1.3</td>
<td>0.09 ± 0.01</td>
<td>8.8 ± 0.8</td>
<td>5.4 ± 0.7</td>
<td>6.6 ± 0.7</td>
<td>28.0 ± 3.0</td>
</tr>
<tr>
<td>May</td>
<td>12.0 ± 1.0</td>
<td>0.10 ± 0.01</td>
<td>9.9 ± 0.6</td>
<td>5.7 ± 0.7</td>
<td>6.7 ± 0.7</td>
<td>40.0 ± 6.9A</td>
</tr>
<tr>
<td>June</td>
<td>12.3 ± 1.0</td>
<td>0.12 ± 0.02</td>
<td>8.1 ± 0.6</td>
<td>5.4 ± 0.6</td>
<td>7.0 ± 0.8</td>
<td>31.9 ± 3.0</td>
</tr>
<tr>
<td>July</td>
<td>13.0 ± 1.2</td>
<td>0.08 ± 0.01</td>
<td>8.7 ± 0.5</td>
<td>4.9 ± 0.4</td>
<td>7.8 ± 0.7</td>
<td>31.9 ± 4.7</td>
</tr>
<tr>
<td>August</td>
<td>12.4 ± 1.1</td>
<td>0.09 ± 0.02</td>
<td>7.9 ± 0.4</td>
<td>5.1 ± 0.6</td>
<td>6.4 ± 0.6</td>
<td>22.4 ± 3.9a,b</td>
</tr>
<tr>
<td>September</td>
<td>11.7 ± 1.1</td>
<td>0.08 ± 0.01</td>
<td>8.8 ± 0.7</td>
<td>5.5 ± 0.5</td>
<td>6.7 ± 0.5</td>
<td>29.7 ± 5.5</td>
</tr>
<tr>
<td>October</td>
<td>11.9 ± 1.0</td>
<td>0.08 ± 0.01</td>
<td>8.7 ± 0.7</td>
<td>4.9 ± 0.6</td>
<td>7.9 ± 0.8</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 1.

Peripheral serum hormone concentrations (mean ± SE) over a period of 13 months. Statistical analysis was done by Duncan’s new multiple range test. The capital and the small form of the same letter indicate a statistically significant difference between these points (P < 0.05).
Results

The peripheral serum concentrations of melatonin, FSH, LH, Prl, testosterone and oestradiol over the period of 13 months are depicted in Table 1. No significant changes were seen in circulating pituitary and testicular hormone concentrations over this observation period. However, two peaks were seen in serum melatonin levels, in December and in May, and nadir values were observed in March and August.

In order to eliminate the influence of the considerable interindividual variability of the absolute hormone concentrations, the monthly hormone levels were converted to percentages of the individual annual means (Fig. 1). Comparisons of these values revealed significant annual variation in all hormones measured, with the exception of testosterone. The May peak of melatonin was associated with significantly increased FSH and LH levels, and the nadir values of melatonin and all pituitary hormones were seen in August. The peak levels of Prl were recorded in October and January, being significantly higher than those in November and August. Serum oestradiol peaked in April and June and reached the lowest value in October.

Positive correlations were found between the concentrations of FSH and LH ($r = 0.41, P < 0.01$), and Prl and LH ($r = 0.26, P < 0.01$). On the other hand, negative correlations were recorded between Prl and testosterone ($r = -0.17, P < 0.01$).

Discussion

The present results indicate significant annual variation in peripheral serum levels of melatonin, pituitary hormones (LH, FSH and Prl) and oestradiol in young adult men. The most striking fluctuation was found in daytime melatonin concentrations, with peak values in December and May, which is in accordance with the results of Arendt et al. (1979). These authors found a significant annual variation in midnight and early morning samples and a similar trend was also recorded in midday values. However, this bimodal annual rhythm appears to be independent of exposure to daylight, suggesting that factors other than light may be involved in the regulation of pineal gland function. On the other hand, the presence of artificial light may mask the possible effect of

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**Fig. 1.**

Peripheral serum hormone levels (mean ± se) calculated as percentages of the individual annual means. The capital and the small form of the same letter indicate a statistically significant difference between these points ($P < 0.05$). The testosterone data have been reported previously (Huhtaniemi et al. 1982).

N-acetyl-5-methoxytryptophan. The sensitivity of the assay was 18 pmol/l. Intra- and inter-assay CV:s were 6.7–9.5 and 9.8–12.5%, respectively.

All the samples from a single subject were analyzed in the same assay, to avoid the influence of inter-assay variation in the month to month changes monitored.

Statistical analysis of the results was carried out by using Duncan's new multiple range test (Steel & Torrie 1960).

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natural light on melatonin secretion. Furthermore, it must be pointed out that in this study the samples were taken in the day time and a possible annual variation in the amplitude of the circadian rhythm of melatonin secretion cannot be excluded.

The mean absolute values of the pituitary hormone concentrations revealed no changes, due to the large interindividual variation (Table 1). However, when expressed as percentages of the individual annual means, several significant changes were found. The peak values of LH and FSH were seen in May, concomitantly with maximal melatonin secretion, and all these hormones showed a nadir in August. This is in contrast to the suppressive effect of melatonin on gonadotrophin secretion demonstrated in animals (Mas et al. 1979). In pubertal boys some authors (Silman et al. 1979; Waldhauser et al. 1984) but not all (Lenko et al. 1982) have shown that activation of pituitary-testicular function is associated with decreased serum daytime (Silman et al. 1979) and nighttime (Waldhauser et al. 1984) melatonin concentrations, in accordance with the results of animal experiments but in adult men no change in gonadotrophin secretion was induced by melatonin administration (Fideleff et al. 1976; Weinberg et al. 1980). It is therefore clear that further investigation is needed before the relationship between these endocrine functions can be fully understood.

Although the peak hormone levels measured appeared during months of increasing daylight (spring and early summer), no obvious relationships between the changes of daytime hormone levels and the amount of daylight were seen. The amplitudes of the variations were similar to those in previous reports from central Europe (Reinberg et al. 1978) and appeared not to be enhanced by the larger annual variation in the amount of daylight. The amount of artificial light in modern society may even out geographical differences. It is therefore possible that the circannual changes observed in the present study, and also in previous studies, are due to some other seasonal factors, including perhaps diet, mood, amount of mental stress, and extent of physical exercise.

References


Vakkuri O, Leppäl uoto J & Vuolteenaho O (1984): Development and validation of a melatonin radioimmuno-


Received on December 15th, 1984.