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Seasonal Variations in Melatonin Secretory Rhythms in High-, Middle-, and Low-Latitude Regions

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Abstract. This study aims to measure the daily melatonin secretory rhythms of people living in high-, mid-, and low-latitude regions characterised by different day lengths and global solar-radiation conditions. In Poland, a high-latitude region, the amount of melatonin secretion is greater, with secretion occurring earlier (exemplifying phase advance). On the other hand, in Vietnam, a low-latitude region, the level is lower and occurs later (phase delay). Japan, a mid-latitude region, shows behaviour intermediate between these two. Melatonin secretory rhythm in Vietnam is closely related to Day length and Global Solar Radiation, though no such relationship is observed in Poland or Japan, making it necessary for other factors to be considered. The results of this study have important implications considering the impacts of light pollution and lighting-related conditions of modern life.

Keywords: melatonin, chronobiology, circadian rhythm, seasonality, lighting conditions, latitude.

Introduction

In the course of evolution, human beings acquired biological rhythms as a survival mechanism by which to adapt to various environmental factors that change daily as well as seasonally. A typical example is the circadian rhythm, which has a cycle of approximately 24 h and regulates sleep-wake timing and the secretion of various hormones. Light is a typical zeitgeber that entrains the circadian rhythm, an innate mechanism in humans, with social time.

Information about the light environment is primarily received via melanopsin-expressing retinal ganglion cells (mRGCs) on the retina of the eye, and transmitted through the retino-hypothalamic tract (RHT) to the suprachiasmatic nucleus (the "clock" that governs biological rhythms), and finally to the pineal gland. The latter secretes melatonin and is very much influenced by the information received. Typically, melatonin secretion begins in the evening, peaks at night, declines in the morning, and falls off almost entirely during the day. The process is modulated solely by light, an environmental factor, and not by human activity, diet, or psychological factors. Therefore, melatonin is a useful indicator for those seeking to study the effects of light on the human circadian rhythm (Reiter, 1993).

It has, for example, been shown that exposure to morning light advances the melatonin secretory rhythm, while night light delays it (Lewy, 2007). In contrast, the light received during the daytime increases night-time melatonin secretion, influencing rhythmic amplitude.

In nature, day length (photoperiod) and global solar radiation considerably affect the phase and amplitude of melatonin rhythm, and there are seasonal fluctuations in melatonin secretory behaviours. However, the results of studies on seasonal fluctuation have remained inconsistent, with some indications that melatonin secretion is higher in winter and lower in summer (Kivela et al., 1988; Stokkan & Reiter, 1994), even as others report the opposite (Touitou et al., 1984), and still others no seasonal fluctuation at all (Sack et al., 1986; Cutler et al., 1995; Morera & Abreu, 2006).

On the other hand, it has been reported that there is no seasonal difference in total melatonin secretion, albeit with the phase advancing in summer compared with winter (Illnerova et al., 1985; Kennaway & Royles, 1986; Honma et al., 1992; Vondrasova et al., 1997; Yoneyama et al., 1999; Zerbini et al., 2021).

Honma et al. (1992) reported that night-time peak melatonin secretion occurs earlier in summer than in winter, while Vondrasova et al. (1997) reported that the morning decrease in melatonin secretion occurs earlier in summer than in winter. Although there are differences between night time and morning, all of these authors found that the melatonin secretory rhythm appeared to advance in summer compared to winter, with this being attributed to the entrainment effect of bright summer morning light on the biological rhythm.

Wehr (1991), Wehr et al. (1993) and Stothard et al. (2017) reported earlier melatonin onset and later melatonin offset in winter compared with summer, resulting in a longer duration of melatonin secretion in winter.

These differences in melatonin behaviour between summer and winter can be attributed to differences in day length. In summer, both advance and delay in the melatonin secretory phase are caused by bright light in the mornings and evenings. Conversely, the late sunrise in winter may disrupt the melatonin secretion entrainment mechanism, possibly causing phase delay. The differences in light quality, quantity, and reception timing may have a counterbalancing effect. The remaining factors with a large influence on the circadian rhythm are likely to shift the rhythm one way or another.

The observed dynamics may result from differences in participants' race and lifestyle, as well as latitude, climate and seasonal timings.

Against such a background, the work detailed here has aimed to measure the daily melatonin secretory rhythms of people living in high-, mid-, and low-latitude regions of different day lengths and global solar-radiation conditions, and to examine the effects of region and season.

Methods

The study was conducted in Warsaw, Poland (high-latitude, 52°N, n = 15), Fukuoka, Japan (mid-latitude, 33°N, n = 14), and Hanoi, Vietnam (low-latitude, 21°N, n = 15), on healthy, city-dwelling male and female adults aged 21-33.

The research was approved by the Ethics Committee at Fukuoka Women's University, and subjects gave their written informed consent prior to the work being carried out. They were also paid for their participation.

Data was collected over five days from Monday to Friday each season, including at the time of the winter solstice, the vernal equinox in spring, the summer solstice, and the autumnal equinox. During each data-collection period, subjects were asked to follow their normal lifestyle, avoid vigorous exercise and excessive alcohol consumption, rise at 7:00 a.m., and retire at 11:00 p.m.

Table 1 shows the latitude, sunrise, and sunset times of the three study areas and the times of rising and retiring among the subjects. The lighting environment they experienced was basically based on natural light from sunrise to sunset, as well as artificial lighting provided for the rest of the time.

To determine melatonin secretory rhythms, subjects were asked to put their saliva into a collection tube known as a Salivette (Sarstedt, Rommelsdorf, Germany) every 3 h from 10:00 a.m. on Thursday to 7:00 a.m. on Friday during the experimental period, at 10:00, 13:00, 16:00, 19:00, and 22:00 h on Thursday and 1:00, 4:00, and 7:00 h on Friday morning, for a total of eight samples. On Fridays at 1:00 and 4:00 h, subjects woke up in the middle of their sleep and collected saliva in dark conditions. Prior to the experiment, subjects were told how to collect the saliva using the Salivettes, and instructed not to eat, drink, or brush their teeth for 90 minutes before saliva collection, as well as to rinse their mouths with water 30 minutes in advance of that. The saliva samples were stored frozen at-20°C prior to the melatonin analysis of saliva involving ELISA (ELISA kit Buhlmann Laboratories AG Swiss).

Statistical analysis entailed one-way and two-way analysis of variance (ANOVA) followed by Tukey post hoc tests, and multiple regression analysis.

Table 1. Latitudes, sunrise and sunset times in the three regions, along with times of rising and retiring among the subjects

Region	Season	Sunrise	Sunset
Poland (Warsaw)	Winter	7:44	15:26
52°N	Spring	5:34	17:52
	Summer	3:14	20:01
	Autumn	5:21	17:32
Japan (Fukuoka)	Winter	7:20	17:16
33°N	Spring	6:20	18:31
	Summer	5:09	19:31
	Autumn	6:05	18:13
Vietnam (Hanoi)	Winter	6:30	17:23
21°N	Spring	6:00	18:09
	Summer	5:17	18:40
	Autumn	5:45	17:52
Experiment schedule		Get-up 7:00	Retire 23:00

Results

The melatonin secretory rhythms by season in the three regions are as shown in Figure 1. Melatonin secretion decreased in Polish subjects in winter, while increasing considerably in Japanese subjects in autumn, as compared with the other seasons. In the case of Vietnam, it was not possible to note significant seasonal differences in melatonin secretion.

To understand melatonin secretory rhythms in detail, spline interpolation was used to calculate peak secretion level and timing, as an index reflecting rhythm amplitude and phase, respectively. The results are shown in Table 2, their relationships in Figure 2. In addition, the area under the curve (AUC) was calculated using the formula after Riemann et al. (2002), to provide an index of total melatonin secretion per day (Fig. 3).

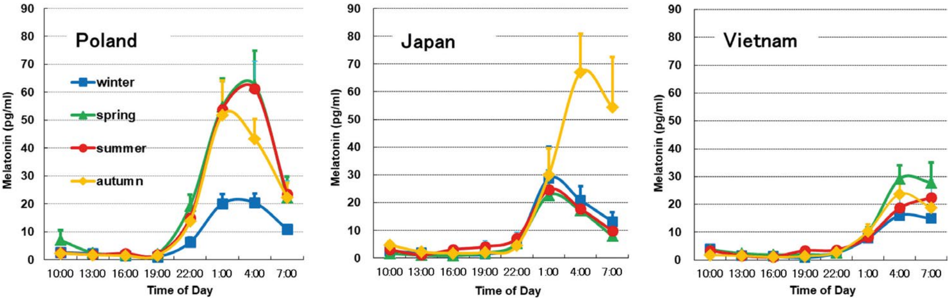

Fig. 1. The melatonin secretory rhythms by season in the three regions

Table 2. Peak level, timing, and area under the curve (AUC) of melatonin secretion, as against day lengths and global solar radiation by season in the three regions

		Peak level (pg/ml) (mean±SD)	Peak timing (h) (mean±SD)	AUC (pg/day) (mean±SD)	Day Length (min)	Global Solar Radiation (MJ/m^2/day)
Poland	Winter	21.9±12.1	2.0±4.0	175.1±88.7	462	0.8
	Spring	63.2±42.2	2.4±1.3	476.1±305.2	732	9.5
	Summer	58.0±35.4	2.6±1.1	447.6±262.3	1007	17.5
	Autumn	50.1±32.5	2.4±1.4	378.2±221.8	732	9.1
Japan	Winter	27.5±27.0	3.9±1.5	202.6±180.2	596	7.4
	Spring	23.1±22.4	2.8±1.7	174.5±149.0	729	8.7
	Summer	26.6±16.5	3.1±1.9	219.8±119.5	864	14.4
	Autumn	72.0±50.2	4.3±2.0	408.5±194.9	729	11.0
Vietnam	Winter	18.6±13.6	4.9±2.4	120.1±59.9	651	18.8
	Spring	30.1±22.4	5.2±1.6	186.5±101.2	728	20.2
	Summer	24.2±18.3	4.8±2.4	149.5±72.8	805	37.0
	Autumn	23.0±17.3	4.4±1.9	155.3±81.7	728	26.6

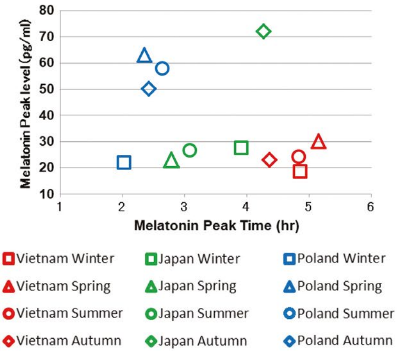

Fig. 2. Relationship between peak level and timing of melatonin secretion by season in the three regions

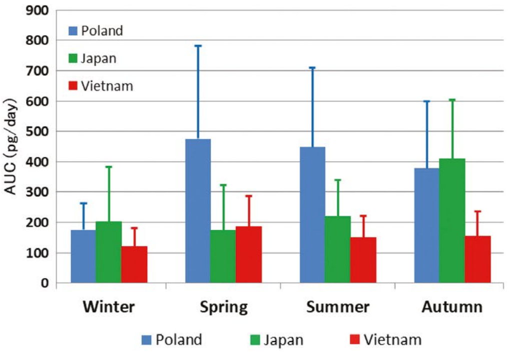

Fig. 3. Area under the curve (AUC) for melatonin secretion by season in the three regions

Results from statistics on seasonal differences in melatonin secretory rhythms in the three regions

The differences in melatonin secretion by season in Poland, Japan, and Vietnam were analysed using with-in one-way ANOVA and the post-hoc test, the results of that being summarised in Table 3.

A) Poland

Statistically significant differences in peak melatonin secretion level and AUC were observed between seasons (p = 0.005, 0.004), and post-hoc test results show that melatonin secretion in winter is at a significantly lower level than in either spring ($p \leqq 0.01$) or summer ($p \leqq 0.05$). In addition, no significant difference between seasons was observed when it came to the time of peak melatonin secretion.

B) Japan

Statistically significant differences in peak melatonin secretion level and AUC were noted between seasons ($p \leqq 0.001$). For example, post-hoc test results showed that melatonin

Table 3. Seasonal differences in melatonin secretion in the three regions, as analysed using with-in one-way ANOVA

		Differences by season	Post-hoc test ($p \leqq 0.05$)
Poland	peak level	p = 0.005	Winter < Spring, Summer
	peak timing	n.s.	
	AUC	p = 0.004	Winter < Spring, Summer
Japan	peak level	p < 0.001	Autumn > Spring, Summer, Winter
	peak timing	p = 0.111	
	AUC	p = 0.001	Autumn > Spring, Summer, Winter
Vietnam	peak level	n.s.	
	peak timing	n.s.	
	AUC	n.s.	

secretion in autumn was significantly greater than in other seasons ($p \leqq 0.05$). The time of maximum melatonin secretion tended to differ between seasons ($p = 0.111$), with a slight phase advance in spring and summer and a slight phase delay in autumn and winter.

C) Vietnam

No significant differences in peak melatonin secretion level, timing, or AUC were found between seasons.

Results for statistics on melatonin secretory rhythms between seasons and regions

The rhythms characterising melatonin secretion were compared between seasons and regions using two-way ANOVA (Figs. 3-5).

A) Peak melatonin secretion level

It was possible to note a significant difference in peak melatonin secretion levels among the three regions ($p = 0.003$): Vietnamese subjects had lower levels of melatonin, while Polish subjects produced it in larger amounts. In addition, there was a significant seasonal difference ($p < 0.001$), with more melatonin generated in spring and autumn, and less in winter. An interaction was observed between seasons and regions ($p < 0.001$), with significant increases in spring and summer in Poland, and in autumn in Japan (Fig. 4).

B) Timing of peak melatonin secretion

There was a significant difference in the timing of peak melatonin secretion among the three regions ($p < 0.001$). Peak timing was late in Vietnam (denoting a phase delay) and early in Poland (phase advance). There were no significant differences between seasons, and no interaction either (Fig. 5).

C) AUC

AUC varied significantly by regions ($p < 0.001$), given that it was smaller in Vietnam, and larger in Poland. It also varied with seasons ($p < 0.001$), with a greater area accounted for by autumn, as opposed to winter. Furthermore, an interaction was observed between seasons and regions ($p < 0.001$), denoting significant increase in spring, summer and autumn in Poland, and in autumn in Japan (Fig. 3).

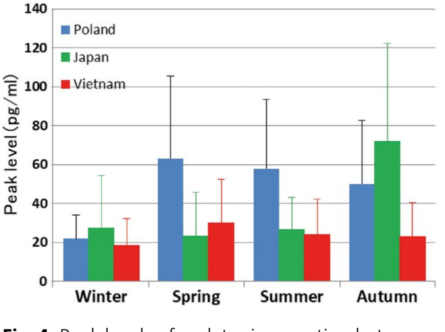

Fig. 4. Peak levels of melatonin secretion between seasons and regions

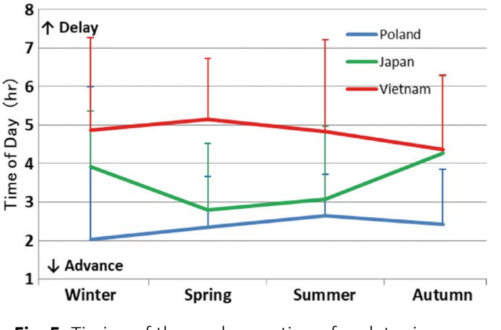

Fig. 5. Timing of the peak secretion of melatonin, between seasons and regions

Discussion

Poland, a country in a high-latitude region, shows an increased peak level of melatonin secretion in people throughout the four seasons, as well as earlier timing of peaks. On the other hand, Vietnam, a country in the low-latitude region, has people who only secrete melatonin at lower peak levels, with the timing of the peak also coming later. In turn, people in Japan, a country in the mid-latitude region, show rhythms to the secretion of melatonin intermediate between those noted for the other two countries. In other words, differences in melatonin-secretion rhythms with a notional move from higher to lower latitudes are characterised by both reduced amplitude and phase delay, as potentially related to a variety of different factors. For our part, the differences investigated were in day length and global solar radiation intensity due to seasonal changes and regional differences in latitude, given a supposition that these might represent the main causes of variation. Day lengths and levels of global solar radiation for the three regions are as shown in Table 2, and the relationship between the two in Figure 6.

In general, there is a positive correlation between day length and global solar radiation, as is shown in Figure 6, though the details of this relationship differ depending on latitude. For example, in high-latitude Poland and mid-latitude Japan, the rate of increase in global solar radiation in line with increased day length is moderate. In contrast, in the low-latitude region of Vietnam, although the difference in day length between the four seasons is small, the increase in global solar radiation in response to an increase in day length is significantly larger.

This difference in correlation may have different effects on peak levels of melatonin secretion, and on the timing to be noted in people from the three different regions.

Multiple regression analysis was performed, treating day length and global solar radiation as variables explanatory in relation to melatonin-secretion rhythms from region to region, with peak melatonin-secretion level, timing and AUC as criterion variables. The effects of the explanatory variables are as summarised in Table 4 as discussion considers positive and negative standardised regression coefficients on the criterion variables, peak level and timing of melatonin secretion, and AUC.

In Poland, changes in peak level and AUC might be explained in terms of a negative relationship with day length (p = 0.26, 0.24) and a positive relationship with Global Solar

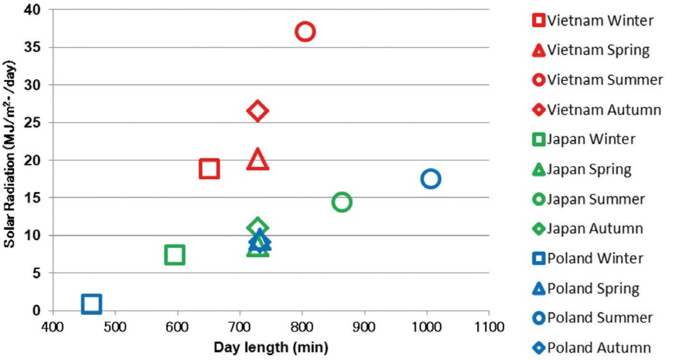

Fig. 6. The relationships between day length and global solar radiation characteristic for the three regions studied

Table 4. The effect of day length and global solar radiation on peak level, timing and AUC of melatonin secretion in the three regions

	Criterion variables	Standardised regression coefficient of explanatory variables	
		day length	Global Solar Radiation
Poland	peak level	-17.3 (p = 0.26)	+18.2 (p = 0.25)
	peak timing	n.s.	n.s.
	AUC	-16.8 (p = 0.24)	+17.6 (p = 0.23)
Japan	peak level	n.s.	n.s.
	peak timing	n.s.	n.s.
	AUC	n.s.	n.s.
Vietnam	peak level	+2.2 (p = 0.01)	-2.0 (p = 0.01)
	peak timing	n.s.	n.s.
	AUC	+2.2 (p = 0.13)	-2.0 (p = 0.15)

Radiation (p = 0.25, 0.23). Conversely, in Vietnam, an increase in day length is associated with an increase in peak level (p = 0.01) and AUC (p = 0.13), and an increase in Global Solar Radiation with a decrease in peak level (p = 0.01) and AUC (p = 0.15). Changes in peak timing in Poland and Vietnam, and changes in peak level, peak timing and AUC in Japan could not be explained by reference to day length and Global Solar Radiation. It is thus necessary to seek factors other than day length and Global Solar Radiation in explaining the criterion variables.

As seen in the spring and autumn in the three regions (even where day length is almost the same), there are large differences in the peak level of melatonin secretion and in its timing. They may be related to the effects of light history, meaning an impact of different spring and autumn lighting conditions after winter and summer, respectively, as was pointed out by Owen & Arendt (1992), Hébert et al. (2002) and Higuchi et al. (2007a).

In addition, as Czarnecka et al. (2021) indicated, consideration needs to be given to differences in the stimulation of mRGCs as a main photoreceptor for circadian rhythm, caused by different lighting conditions in Fukuoka and Warsaw, the relationship between the spectrum energy distribution of light by time of day and season in the region, and the spectral sensitivity distribution of mRGCs.

Ueno-Towatari et al. (2007) reported a higher and later peak level for secretion of melatonin in autumn as compared with other seasons in Japan, as an individual report. Błażejczyk et al. (2014) also compared seasonal variation in melatonin-secretion rhythms in Japan and Poland in relation to light environmental conditions in each region. They pointed to the possibility of local light quality having a significant effect, with that denoting that different wavelengths of light have different effects on melatonin behaviour.

In addition, as was shown by Higuchi et al. (2007b), race-related differences may be another factor explaining differences in secretory rhythms. The factors mentioned above may be involved in melatonin secretory rhythms, and as such represent potential topics for future research.

Regarding the gender difference, the subjects in our experiment were healthy male and female adults aged 21-33. Some reports have indicated higher levels of melatonin in females than males (Fideleff et al., 2006; Burgess & Fogg, 2008; Cain et al., 2010), while another indicated that there was no gender difference in melatonin suppression by light (Nathan et al., 2000). Although it is not clear how these factors affect this study, we considered it might be quite straightforward to confirm seasonal variations in the same subjects in this experiment. This must represent a future research topic, however, with a large number of research subjects.

This study is an extension of the two papers; Ueno-Towatari et al. (2007) and Błażejczyk et al. (2014), and has aimed to compare the seasonal variation in melatonin secretory rhythms among people living in high-, mid-, and low-latitude regions – a comparison achieved by adding in the Vietnamese data to the previous results from Poland and Japan, and by investigating the light conditions characteristic of each region.

In modern life, our melatonin rhythms are affected by the fluctuations in natural light and artificial lighting in our lifestyle. However, it is very difficult to distinguish and grasp the effects of these on the results. In this study, melatonin secretory rhythms under these influences were encapsulated by reference to regional and seasonal differences. The results obtained were considered mainly from the viewpoint of natural light, given that the relationship between melatonin and natural light was constructed in the process of evolution, and thus regarded as more robust than the relationship between melatonin and artificial lighting, basically a phenomenon of the last 100-150 years, as a reflection of a "modern" human lifestyle.

It is also true that in modern society the change from natural to artificial light sources, and the shift to a nocturnal lifestyle, have disrupted the timing of light reception, and altered light-related conditions in people's daily lives. As a result, days are darker, and nights are brighter compared with natural conditions, the impact of this on circadian rhythm being considerable. In apparent consequence, there are increased incidences of physiological and psychological disorders, such as sleep disorders, obesity, cancer risk and depression (Roenneberg & Foster, 1997; Duffy & Wright, 2005; Roenneberg et al. 2007; 2013).

The results of this study, which showed the basic behaviours of melatonin secretion in high-, mid-, and low-latitude regions by season, have important implications for those considering the impacts of light pollution and the lighting-related conditions of modern life.

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