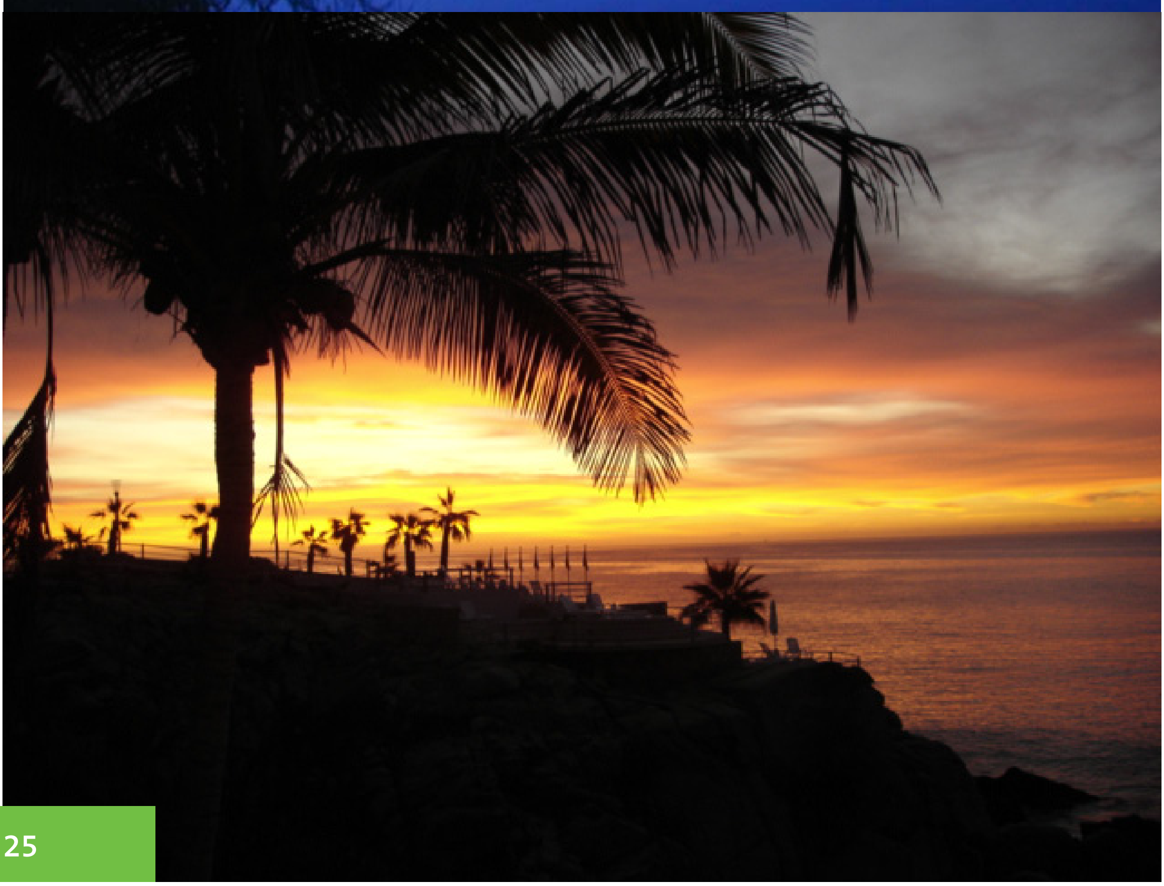
NATIONAL INSTITUTE
FOR HEALTH AND WELFARE

RESEARCH

Sharon Grimaldi Toriz

Epidemiological Data of Seasonal Variation in Mood and Behaviour



25

National Institute for Health and Welfare
Department of Mental Health and Substance Abuse Services
Helsinki, Finland
and
University of Helsinki
Department of Public Health
Helsinki, Finland

RESEARCH

Sharon Grimaldi Toriz

Epidemiological Data of Seasonal Variation in Mood and Behaviour

ACADEMIC DISSERTATION

To be presented with the permission of the Faculty of Medicine, University of Helsinki, for public examination in Lecture hall 1, Department of Public Health, Mannerheimintie 172, Helsinki, on December 18th, 2009 at 12:00.

Cover photos: Sharon Grimaldi Toriz

ISBN 978-952-245-178-1 (print)
ISBN 978-952-245-179-8 (pdf)
ISSN 1798-0054 (print)
ISSN 1798-0062 (pdf)

Helsinki University Print
Helsinki, Finland 2009

Supervised by
Docent Timo Partonen, MD, PhD
Department of Mental Health and Substance Abuse Services
National Institute for Health and Welfare

and

Professor Jouko Lönnqvist, MD, PhD
Department of Mental Health and Substance Abuse Services
National Institute for Health and Welfare
and
Department of Psychiatry
University of Helsinki

Reviewed by
Professor Sari Lindeman, MD, PhD
Department of Psychiatry
University of Oulu

and

Professor Jukka Hintikka, MD, PhD
Department of Psychiatry
University of Kuopio

Opponent
Professor Vincenzo Natale, MD, PhD
Department of Psychology
University of Bologna

"For everything there is a season, and a time for every purpose over the heaven..."
- Ecclesiastes.

Table of contents

Abstract

Sharon Grimaldi Toriz, Epidemiological Data of Seasonal Variation in Mood and Behaviour
Publications of the National Institute for Health and Welfare, Research 25/2009, 114 Pages
ISBN 978-952-245-178-1 (print), ISBN 978-952-245-179-8 (pdf)

The aim of this study was to measure seasonal variation in mood and behaviour. The dual vulnerability and latitude effect hypothesis, the risk of increased appetite, weight and other seasonal symptoms to develop metabolic syndrome, and perception of low illumination in quality of life and mental well-being were assessed. These variations are prevalent in persons who live in high latitudes and need balancing of metabolic processes to adapt to environmental changes due to seasons.

A randomized sample of 8028 adults aged 30 and over (55% women) participated in an epidemiological health examination study, The Health 2000, applying the probability proportional to population size method for a range of socio-demographic characteristics. They were present in a face-to-face interview at home and health status examination. The questionnaires included the modified versions of the Seasonal Pattern Assessment Questionnaire (SPAQ) and Beck Depression Inventory (BDI), the Health Related Quality of Life (HRQoL) instrument 15D, and the General Health Questionnaire (GHQ). The structured and computerized Munich Composite International Diagnostic Interview (M-CIDI) as part of the interview was used to assess diagnoses of mental disorders, and, the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) criteria were assessed using all the available information to detect metabolic syndrome.

A key finding was that 85% of this nationwide representative sample had seasonal variation in mood and behaviour. Approximately 9% of the study population presented combined seasonal and depressive symptoms with a significant association between their scores, and 2.6% had symptoms that corresponded to Seasonal Affective Disorder (SAD) in severity. Seasonal variations in weight and appetite are two important components that increase the risk of metabolic syndrome. Other factors such as waist circumference and major depressive disorder contributed to the metabolic syndrome as well. Persons reported of having seasonal symptoms were associated with a poorer quality of life and compromised mental well-being, especially if indoors illumination at home and/or at work was experienced as being low. Seasonal and circadian misalignments are suggested to associate with metabolic disorders, and could be remarked if individuals perceive low illumination levels at home and/or at work that affect the health-related quality of life and mental well-being.

Keywords: depression, health-related quality of life, illumination, latitude, mental well-being, metabolic syndrome, seasonal variation, winter.

Tiivistelmä

Sharon Grimaldi Toriz, Mielialan ja käyttäytymisen vuodenaikaisvaihtelun epidemiologisia tietoja
Terveyden ja hyvinvoinnin laitoksen julkaisuja, Tutkimus 25/2009, 114 sivua
ISBN 978-952-245-178-1 (print), ISBN 978-952-245-179-8 (pdf)

Tämän tutkimuksen aiheena oli mielialassa ja käyttäytymisessä ilmenevän vuodenaikaisvaihtelun merkitys terveydelle. Tämä kaamosoireilu altistaa metaboliselle oireyhtymälle, jonka ilmaisimena kaamosoireet voisivat toimia osana terveystarkastuksia. Kaamosoireet johtuvat elimistön sisäisen kellon rytmihäiriöistä. Kaamosoireita voi lievittää ja ehkäistä paitsi liikunnalla myös valolla. Elimistön sisäistä kelloa tahdistava valaistus saattaisi edistää painonhallintaa ja edelleen ehkäistä metabolista oireyhtymää. Yleisvalaistuksen kohentaminen saattaisi lisäksi vaikuttaa myönteisesti niin terveyteen liittyvään elämänlaatuun kuin henkiseen hyvinvointiin.

Tutkimuksen lähdeaineistona käytettiin Terveys 2000 -tutkimusta. Sen 30-vuotiaita ja sitä vanhempia suomalaisia edustavaan otokseen kuului 8028 henkilöä. Heistä 5480 haastateltiin kasvokkain, minkä jälkeen heidän terveydentilansa tutkittiin ja he vastasivat muokatun vuodenaikaiskyselyn (Seasonal Pattern Assessment Questionnaire), muokatun mielialakyselyn (Beck Depression Inventory), geneerisen terveyteen liittyvän elämänlaatukyselyn (15D) ja henkisen pahoinvointikyselyn (General Health Questionnaire) kysymyksiin. Mielenterveyden häiriöiden diagnosoimiseksi käytettiin strukturoitua menetelmää (Munich Composite International Diagnostic Interview), ja metabolisen oireyhtymän määrittämiseksi käytettiin National Cholesterol Education Program Adult Treatment Panel III:n mukaisia kriteerejä.

Tämä tutkimus osoitti, että 85 sadasta suomalaisesta kokee mielialansa ja käyttäytymisensä toistuvasti vaihdelleen vuodenaikojen mukaan. Kolmella sadasta nämä kaamosoireet ovat olleet siinä määrin vakavia, että he hyötyisivät hoidosta. Yhdeksällä sadasta oli tutkimustalvena yhtaikaa sekä vakavia masennusoireita että vakavia kaamosoireita, ja jos aiempien tutkimusten havainnot siitä, että joka kymmenes tällainen henkilö sairastaa kaamosmasennusta, pätevät tähän tutkimukseen, niin kaamosmasennuksen esiintyvyys suomalaisilla on 9 tuhannesta. Vakavien kaamosoireiden esiintyminen suurensi riskin samanaikaisten vakavien masennusoireiden ilmenemiselle yli kolminkertaiseksi. Niin kaamosoireet kuin masennusoireet vallitsivat tasaisesti maassamme.

Kaamosoireista erottui kaksi faktoria: metabolinen faktori ja mielenterveyden faktori. Edelliseen lukeutuivat painossa ja ruokahalussa ilmenevät vuodenaikaisvaihtelut. Kaamosoireiden vahva latautuminen vuodenaikaisvaihtelun metaboliselle faktorille suurensi metabolisen oireyhtymän vaarasuhteen 1.2-kertaiseksi ja selittyi merkitsevästi osaltaan myös huonoksi koetusta kodin yleisvalaistuksesta käsin. Etenkin painon toistuva vuodenaikaisvaihtelu osoittautui metabolisen oireyhtymän uudeksi riskitekijäksi jo tunnettujen riskitekijöiden huomioimisen jälkeenkin. Heikompi terveyteen liittyvä elämänlaatu selittyi merkitsevästi niin kaamosoireilla kuin huonoksi koetulla yleisvalaistuksella ja ne selittivät merkitsevästi myös suurempaa henkistä pahoinvointia vielä tunnettujen riskitekijöiden huomioimisen jälkeenkin.

Elimistön sisäisen kellon toiminnasta syntyvissä vuodenaikaisvaihteluissa ja vuorokausirytmeissä ilmenevät rytmihäiriöt saattavat johtaa metabolisiin häiriöihin. Nämä metaboliset häiriöt voivat edelleen pahentua niukan valaistuksen seurauksena mutta toisaalta lievittyä valoaltistuksen avulla. Siten sisäisen kellon rytmihäiriöt ja valo vaikuttavat terveyteemme, mikä ilmenee muun muassa terveyteen liittyvässä elämänlaadussa ja henkisessä hyvinvoinnissa.

Avainsanat: elämänlaatu, hyvinvointi, kaamosoire, leveyspiiri, masennustila, metabolinen oireyhtymä, valaistus, vuodenaika

Abbreviations

15D	The 15D health-related quality of life instrument
BDI	Beck Depression Inventory
BMI	Body-Mass Index
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
GHQ-12	General Health Questionnaire, 12-item version
GSS	Global Seasonality Score
HDL-C	High-Density Lipoprotein Cholesterol
HRQoL	Health-Related Quality of Life
LDL	Low-Density Lipoprotein
M-CIDI	Munich Composite International Diagnostic Interview
NCEP-ATPIII	National Cholesterol Education Program Adult Treatment Panel III
NREM	Non Rapid Eye Movement
QoL	Quality of Life
REM	Rapid Eye Movement
SAD	Seasonal Affective Disorder
SCN	Suprachiasmatic Nuclei
SNS	Sympathetic Nervous System
SPAQ	Seasonal Pattern Assessment Questionnaire
Sub-SAD	Subsyndromal Seasonal Affective Disorder
TG	Triglyceride
WHO	World Health Organization
WHR	Waist to Hip Ratio

List of original publications

This thesis is based on the following original publications, which are referred to in the text by Roman numerals I-IV.

I. **Grimaldi S**, Partonen T, Haukka J, Aromaa A, Lönnqvist J. Seasonal vegetative and affective symptoms in the Finnish general population; Testing the dual vulnerability and latitude effect hypotheses. Nordic Journal of Psychiatry. 2009; 63: 397-404. doi:10.1080/08039480902878729

II. Rintamäki R, **Grimaldi S**, Englund A, Haukka J, Partonen T, Reunanen A, Aromaa A, Lönnqvist J. Seasonal changes in mood and behavior are linked to metabolic syndrome. PLoS ONE. 2008; 3(1): e1482. doi:10.1371/journal.pone.0001482.

III. **Grimaldi S**, Englund A, Partonen T, Haukka J, Pirkola S , Reunanen A, Aromaa A, Lönnqvist J. Experienced poor lighting contributes to the seasonal fluctuations in weight and appetite that relate to the metabolic syndrome. Journal of Environmental and Public Health. 2009; vol. 2009, Article ID 165013, 11 pages. doi:10.1155/2009/165013.

IV. **Grimaldi S**, Partonen T, Saarni S, Aromaa A, Lönnqvist J. Indoors illumination and seasonal changes in mood and behavior are associated with the health-related quality of Life. Health and Quality of Life Outcomes. 2008; 6: 56. doi:10.1186/1477-7525-6-56.

In addition some unpublished data is reported.

1 Introduction

The principle and role of light in our lives is so essential that deserves to be explained by using a metaphor called "The Alaskan Myth from the Inuit" (http://www.ilhawaii.net/ ~stony/ lore12.html):

"In the early times, there was only darkness; there was no light at all. At the edge of the sea, a woman lived with her father. One time she went out to get some water. As she was scraping the snow, she saw a feather floating toward her. She opened her mouth and the feather floated in and she swallowed it. From that time she was pregnant. Then she had a baby. Its mouth was a raven's bill. The woman tried hard to find toys for her child. In her father's house was hanging a bladder that was blown up. This belonged to the woman's father. Now the baby, whose name was Tulugaak (Raven), pointed at it and cried for it. The woman did not wish to give it to him but he cried and cried. At last she gave in and took the bladder down from the wall and let the baby play with it. But in playing with it, he broke it. Immediately, it began to get light. Now there was light in the world, and darkness, too. When the woman's father came home, he scolded his daughter for taking the bladder down from the wall and giving it to the child. And when it was light, tulugaak had disappeared".

This myth is conceived as the analogy of the origin of light and its variation with the day-night, the weather as well as the seasons of the year. When living beings are born they are attracted to this powerful energy, and discover its properties due to the fact that it marks their rhythms. Human beings cannot perform their vital activities adequately without it and its benefits on a molecular and behavioural level. The way light is reflected can influence on the look and feel of a home, which makes it a source of health and a work of art by itself. The position of the sun during the day can be used as a tool for architects and designers to manipulate the perception of any interior, giving it the advantage of versatility to create several moods inside rooms.

Persons who live in the tropics are used to receiving the sun every morning, without realizing its importance in human health and well-being. One of the first scientists who studied the effects of light on health was Niels Ryberg Finsen. He was born in 1860 in the Faroe Islands and studied medicine in Copenhagen, but suffered from the Pick's disease. This disease caused organ impairment and Finsen ended his days in a wheelchair. However, he continued to provide valuable research contributions to medicine. He described his experience as follows (http://nobelprize.org/nobel_prizes/medicine/laureates/1903/finsen-bio.html):

"My disease has played a very great role for my whole development... The disease was responsible for my starting investigations on light: I suffered from anaemia and tiredness, and since I lived in a house facing the north, I began to believe that I might be helped if I received more sun. I therefore spent as much time as possible in its rays. As an enthusiastic medical man I was of course interested to know what benefit the sun really gave. I considered it from the physiological point of view but got no answer. I drew the conclusion that I was right and the physiology wrong. From this time (about 1888) I collected all possible observations about animals seeking the sun, and my conviction that the sun had a useful and important effect on the organism (especially the blood?) became stronger and stronger. What this useful effect really was, I could not find; I have been working for this goal ever since but have not been able to find exactly what I have been seeking, though we have gone somewhat forward.

My intention was even then (about 15 years ago) to use the beneficial effects of the sun in the form of sun bathing or artificial light baths; but I understood that it would be inappropriate to bring it into practical use if the theory was not built upon scientific investigations and definite facts.

During my work towards this goal I encountered several effects of light. I then devised the treatment of small-pox in red light (1893) and further the treatment of lupus (1895). Both these things are therefore in a sense side-issues, but they completely occupied my time for several years and have partly drawn me away from my main goal.

During the last few years, I have, however, become convinced that it does not help to wait until I find the answer I am looking for in the laboratory, but that it is justified to work also with clinical experiments. Thus both approaches can be carried out simultaneously in the effort to reach the final goal".

Finsen reported studies about the effects of light on the skin, as well as the use of concentrated chemical light rays in medicine. According to his theory, light could be used to treat diseases and he created a powerful lamp with his name. However, during his time seasonal affective disorder (SAD) was not recognized as a mood disorder caused by a shortened photoperiod. So, it was unknown whether his interest on the benefits of light in living beings might be linked to the application of phototherapy in mood disorders.

At the beginning of autumn the colours of the leaves turn to brownish, yellowish and reddish tones and then start to fall on the ground as a signal of a change not just in the environment, but on mood and behaviour as well. Herbert Kern was an illustrative case of seasonal depression reflected in the content of his pocket notebooks that recorded key moments in his life: *"During the rest of the year, I could fill a notebook every two weeks; in the winter, it would take months".* When Mr Kern heard about the research of melatonin and bright light exposure by Dr Alfred Lewy's research team, he approached them so as to be submitted to light therapy. He continued the prescription at home and it was effective towards his well-being sensation (Bhattacharjee, 2007).

The day-light period has more seasonal difference in higher latitudes than in lower latitudes; when the shorter days of autumn and winter precipitate a syndrome that can consist of depression, fatigue, prolonged sleep, hyperphagia, carbohydrate craving, weight gain and loss of libido. This syndrome is called SAD. Many hypotheses have been given to explain SAD, starting from the biochemical mechanisms behind the predisposition toward this disease, including circadian phase-shifting, abnormal pineal melatonin secretion and abnormal serotonin synthesis. When physiological symptoms (sleep length, appetite and low energy level) are experienced at the beginning of autumn/winter, individuals might develop negative thoughts that become depression, especially if they possess a low self-esteem and an isolated life (McCarthy et al., 2002). Indeed, if these subjects are migrants from the tropics and/or female they predisposed to manifest such symptoms (Michalak et al., 2003).

Seasonal variations in mood and behaviour are called in the literature as seasonal changes, fluctuations, oscillations, rhythms or symptoms as well. Here and onwards, the term seasonal variation is used to describe the phenomena. Previous findings have detected that seasonal variations in weight might predispose to metabolic syndrome, especially in the regulation of blood glucose levels (Heiskanen et al., 2006; McIntyre et al., 2007). It was found that 66% of men were overweight and 20% of the total population were obese. The indicators of metabolic syndrome are abdominal obesity, insulin resistance, high blood pressure, high plasma lipid levels and high urate levels. Adipose tissue function is considered as an indicator of a disorder in circadian rhythms, the principal responsible of physiological and behavioural rhythms in a day. Therefore, biological systems have to adapt to seasonal changes in photoperiod. These rhythms are coordinated by the suprachiasmatic nuclei (SCN) in the brain, regulating hormones, metabolites and body temperature in mammals. The assessment of seasonal symptoms and sleep-wake cycle reflect the function of the circadian pacemaker as behavioural traits.

Nowadays it has become relevant to evaluate quality of life (QoL) and mental well-being in mental disorders. Their role in daily life is basic, so it is required to recognize all physical, emotional and social affections in human beings. Michalak et al. (2007) reported impaired QoL in wintertime, that can be improved with light therapy. Natural daylight helps well-being as well as artificial indoor light with increased lux.

A healthy lifestyle can protect from seasonal variations if practiced regularly (physical exercise). But if addictive substances such as alcohol are used at a regular basis can predispose to such symptoms in autumn. Instead, if it is followed unhealthy habits, partially influence by seasonal variations (increased appetite and carbohydrate craving) waist circumference can increase and appear metabolic syndrome.

2 Review of the literature

2.1 The light as an essential resource of power in the environment

The natural light originating from the sun is the principal electromagnetic radiation component capable of stimulating the human eye and can be reflected from any surface. Thanks to solar radiation, the living beings on earth have been able to evolve and survive on the planet. It varies depending on the transitions from day-night and from summer-winter forming cycles that synchronize biochemical rhythms in human beings (see figure 1). Every chemical reaction is carried out by two kinds of energy: activation and reaction. The first one comes from a radiant source (light) and causes thermodynamic and photochemical reactions. The second is related to the circadian neurological and endocrine regulation. The regions of cells responsible in this complex physiological level are: the SCN, the paraventricular nuclei, the spinal cord, the superior cervical ganglion and the pineal gland that produces melatonin (Green et al., 2008).

Figure 1. Sunlight variations during the day and in the evening.

The light that comes from an artificial source is the result from a transformation of energy by combustion or electricity. This source is commonly used in architecture and urbanism so as to increase the quality of life and social activity in human beings. The characteristics of artificial light are different from natural light. The spectrum of radiation differs from the chromatic reproduction and temperature (Yerushalmi and Green, 2009).

Figure 2. Contrasts between artificial indoor and natural outdoor lighting conditions.

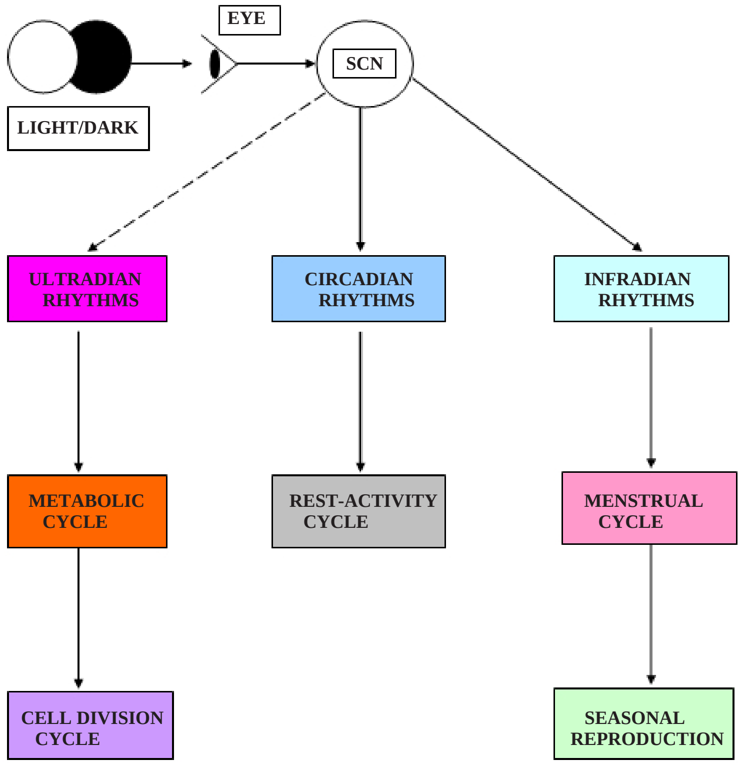
The presence or absence of light and the variation of its characteristics determine and condition persons' behaviour and mood by the visual perception (see figure 2). On the other hand light regulates physiological processes such as biological rhythms, hormonal activity and behaviour. The periodicity of environmental light varies with the time of the day, the season, the year, etc. The geographical factor light-dark and the physical characteristics of our planet determine such variation and synchronize our biological rhythms (Foster and Roenneberg, 2008).

2.2 Circadian rhythms in relation to light and seasonal variation in mood and behaviour

The term circadian rhythm was used for the first time by Dr Franz Halberg in 1959 who described the biological rhythms and their duration of about 24 hours (Halberg et al., 1959; Thorpy and Yager, 1991). These are regular oscillators so that their cycle frequency goes from a millisecond to various years. In other words, circadian rhythms are the consequence of changes of activities along the day of the systems in the organism (Hofstra and de Weerd, 2008). The biological clocks are internal systems that allow the organisms to regulate their internal function and their behaviour. The human body contains multiple systems that work in a cyclical way, such as heart beats, rapid eye movement sleep, menstrual cycles and reproductive behaviour (see figure 3). It is crucial to recognize changes in these rhythms so as to make an accurate diagnosis and treatment for any disorder related to them (McClung, 2007; Monteleone and Maj, 2008; Takahashi et al., 2008).

There are three principal types of biological rhythms: ultradian (shorter than 24 hours), circadian (about 24 hours) and infradian (longer than 24 hours) rhythms (see figure 3). Biological functions in humans such as sleep-wakefulness are regulated by a 24-hour rhythm; body temperature and metabolism are regulated by endocrine and neuronal system. Hormones show daily rhythms in their secretion, such as melatonin and cortisol. Daylight presents variations between day and night and with its impact allows the adaptation of living beings to natural environments; its duration regulates circadian transitions known as "phase advance" or "phase delay". Light enters through the eye involving the synchronization process between the retino-hypothalamic pathways, the suprachiasmatic nuclei, and the pineal gland (Czeisler et al., 1990; Küller et al., 2002; Murguía, 2002).

Figure 3. The action of light on physiological and behavioural cycles in different time rhythms.



Abbreviation: SCN = Suprachiasmatic nuclei.

Melatonin produced in the pineal gland is the key factor to activate the circadian rhythm. It is processed during the night in the darkness, and helps sleep and to recover mentally and physiologically (Rivest et al., 1989). This hormone regulates directly or indirectly the production of hormones in the pituitary (human growth hormone), thyroid and adrenal glands as well as the activity of the immunological system. When bright light appears, melatonin production reduces and the circadian phase shift occurs (Arendt, 1998; Vondrasova et al., 1999).

The synthesis of melatonin in the pineal gland has a central role by coordinating the effect of light through the eyes during day and seasonal variations. During the day its level is very low, increases in the evening and reaches its maximum level during the night. In contrast, cortisol levels increase in the morning and decreases in the evening. The activity of the autonomous nervous systems varies during the day. The production of cortisol in the adrenal cortex follows a circadian rhythm, with a dominating activity during the day. The secretion of melatonin and cortisol vary according to the geographical location either near or far from the equator (Arendt, 1998; Vondrasova et al., 1999). For example, in Southern Sweden it was found that the production of cortisol decreases at the beginning of the autumn and winter and increases at the end of February (Küller and Wetterberg, 1996).

The most important environmental factors that influence on the biological rhythms are the cycles of day-night and light-dark. The mammals have an especial route that conducts information of the light from the retina to the biological clock located in the hypothalamus. Other factors that are product of behaviour have the capacity to act over circadian rhythms such as social interaction, meal time and sleep-wake cycle. These functions can be kept even in complete isolation from the environment, which are called "free running" so they can operate in an independent manner.

Human beings present a circadian time of 24 hours each day with a small change of four minutes, which shows its plasticity, but sleep-wake cycle and its relation to temperature has a steady pattern. When temperature decreases as a result of the transition between day and night, individuals experience the need to sleep. Its origin lies in the nervous system, due to the fact that the physical and intellectual performances such as memory, reaction time, manual skill and alertness have a clear circadian regulation.

Our daily activities are regulated by energetic changes from our inner organs with the environment. Therefore, the actions directly involved with the responses to the environment have the objective to preserve the inner physiological processes and reduce the rhythmical variations. Human beings have evolved to adapt to the most adverse environmental conditions. In order to keep such balance they have developed several control mechanisms. Physiological function is based on time rhythms that vary from less than 24 hours, which are called ultradian rhythms that regulate metabolic and cell division cycles. Circadian rhythms last 24 hours and are in charge of the regulation of the body temperature. Infradian rhythms' duration is more than 24 hours and mark the time of seasonal reproduction, menstrual cycles and seasonal variations in mood and behaviour. These rhythms need external resources such as food (eating-fasting), exercise (rest-activity) and lighting (light-dark) to work harmoniously with the physical environment. Sleeping (REM-NREM stages) is the feedback received when the organism works with the environment (Murguía, 2002; see figure 3).

Homeostasis is defined as diverse strategies that let the organism respond in an appropriate manner to the changes in the environment, which is called reactive homeostasis. Predictive homeostasis can provide corrective responses that anticipate the appearance of environmental stimulus. From the point of view of homeostasis, disease begins when the organism and its regulatory processes are disturbed. Many of these processes are not the product of the disease itself, but an effort of the organism to return to its balance. Therefore, the difference between homeostatic and non-homeostatic response is crucial so as to achieve an accurate diagnosis and treatment to several human diseases. The chronobiologists use a concept called desynchronization that refers to the change of phase of circadian rhythm, which helps to understand how medical treatments work to resynchronize sleep and other disorders. The dissociation among the diverse biological rhythms causes fatigue and lower performance during the day. Any disruption in our daily patterns, the organism presents disorders such as decreased appetite, low mood and depressive symptoms. During the dark periods the circadian rhythm suffers a phase-shift which results in fatigue, hypersomnia and sadness. A large number of individuals experience seasonal symptoms of fatigue from November to February if they reside in the northern hemisphere (Partonen and Lönnqvist, 1998).

A prime example would be the seasonal affective disorder as a disruption in the daily pattern that causes anergia, hypersomnia depression and somatic problems. The annual variation of the amount of light together with inappropriate changes in the circadian rhythms are the principal causes of inactivity during the dark winters. This idea coincides with the hypothesis proposed to explain SAD that the shorter winter photoperiod caused depressive symptoms. This environmental factor may also be responsible in the onset of the vegetative symptoms. Light synchronizes the circadian pacemaker, located in the SCN, and its exposure shifts phases of the circadian rhythms in humans. The time of light exposure regulates the direction and the magnitude of such shifts. SAD and hypersomnia come when circadian phases are delayed relative in coordination to the external clock or to the sleep-wake cycle. Light therapy can correct this phase delay (Lam and Levitan, 2000). Other theories include photoperiod and phase-shift hypotheses, which are still valid in the explanation of the pathophysiology of SAD and seasonality. Nevertheless, other recent findings revealed disturbances in the thermoregulation and electroencephalographic slow-wave sleep in SAD (Sohn and Lam, 2005).

It has been detected seasonal variations affect such as birth rates, body growth, mental attention, sociability, and prevalence of suicide and homicide. During the winter, a large number of sick persons are reported with colds and infections due to low intake of vitamins and exposure to ultraviolet light. Therefore, their physical activity decreases as a result of a circadian disorder (Roenneberg and Aschoff, 1990; Küller and Wetterberg, 1996; Preti, 1997; Tiihonen et al., 1997; Partonen et al., 2004).

Circadian rhythms regulate the approximate 24-hour oscillations in behaviour and physiology, which internally help to anticipate the environmental changes associated with the sunlight. The circadian system is not only organized by the SCN, but also the surrounding tissues and cultured cells in mammals. The interactions among them vary according to the tissue and influence on the overall well-being (Ko and Takahashi, 2006). The circadian clock that regulates behaviour in mammals is located in the SCN of the brain. Recently it was found that circadian clocks are distributed in mammalian tissues, such as retina that is under circadian control. The circadian retina genes are involved in many functions, such as retinal physiology and metabolism but they still remain a mystery. A significant adaptive mechanism reached by circadian rhythms is the capacity to anticipate changes and predict variations in the environment (Storch et al., 2007).

Mood is the result of a complex interaction between circadian phase and the duration of wakefulness. The disrupted circadian cycles in persons with winter SAD are due to inconsistent transmission of serotonin of neuropeptide Y through the different channels that conduct to the circadian pacemaker. The explanatory factors are shorter periods of daylight, exposure to cold weather and ageing (Partonen and Lönnqvist, 1998).

2.3 Prevalence of seasonal variation in mood and behaviour

Increased suicide rates, increased hospital admissions and general practitioner consultations due to affective disorders as well as prescription of antidepressants follow a seasonal pattern (Magnusson, 2000). Lurie et al. (2006) provided an overall lifetime prevalence of SAD which ranges from 0 to 9.7 percent and for major depression with seasonal changes was 0.4 percent. Partonen and Lönnqvist (1998) estimated that 15% of the mood disorders presented a seasonal component and the risk of SAD was between 1-2%. The prevalence of SAD and subsyndromal SAD (sub-SAD), i.e. milder forms of seasonal variations in mood and behaviour, in the Finnish population was 1-3% in 2 years and 2-4% in 3 years. SAD seemed to be less prevalent from the seasonal variations, especially in children and adolescents.

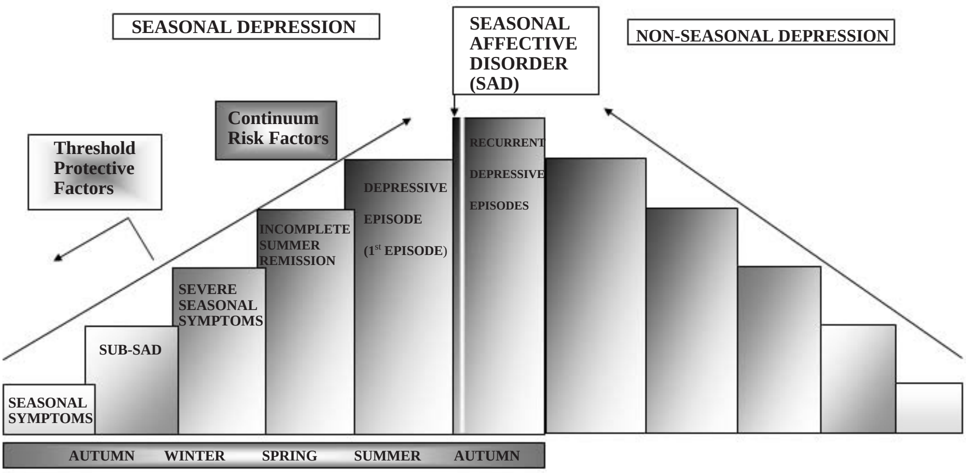
Seasonal symptoms begin in the autumn with the presence of vegetative symptoms and sub-SAD appears as a result. Light and exercise are protective factors that help to prevent further complications. If the subjects let risk factors come into the scenario, such as darkness, sedentarism, lack of social activities and fatigue, severe seasonal changes, incomplete summer remission and even the first depressive episode may occur as a consequence (see figure 4).

SAD appears with recurrent depressive episodes in autumn or winter with or without spring or summer remission (Kasper et al., 1989 b). Women and young individuals are the most affected by the lack of sunlight and lower temperatures in winter. Mersch et al. (1999 a) mentioned that 41% of young women between 26 and 35 years met the criteria of SAD. In addition, they presented more problems in weight fluctuation and increased sleep more in autumn and winter. They spent most of their time indoors with few hours of physical activity. It seems that elder people are not affected by such changes (Magnusson, 2000). Individuals with seasonal problems or SAD might present bipolar pattern in spring/summer, and bulimia nervosa and other eating disorders increases in winter (Magnusson, 2000). Mersch et al. (1999 b) found in the Dutch population a peak pattern in December, 50% more than in July. Reactions towards seasonal changes are considered as "normal" transitions, in which SAD individuals are located on the extreme part of seasonal dimension. They also found that depression was more common in winter than in summer. According to these authors, persons with SAD might present higher risk to suffer of episodes of depressed mood. Winter period is a stressor that increases the risk to make seasonal symptoms worse, due to biological, psychological and social factors.

The estimation of the "real" prevalence of SAD was considered a difficult task due to the spread use in other studies of the Seasonal Pattern Assessment Questionnaire (SPAQ), instead of using reliable standard diagnostic interviews (Michalak et al., 2001). Approximately 2.4% of the UK population might encounter the diagnostic criteria for SAD. It is commonly under-diagnosed by general practitioners, because they confuse them with somatic symptoms (weight gain, fatigue and hypersomnia). When Wicki et al. (1992) performed an epidemiological study of seasonal depression in Zurich, they found various psychiatric and somatic problems in younger women in Switzerland, such as neurasthenia, respiratory complaints, headaches, circulatory difficulties and backache during winter. They also reported the same symptoms as previous studies, such as increased appetite, carbohydrate craving, weight gain and increased sleep. However, they encountered deficiencies in the reliability to find the "true" SAD individuals within the population by applying the SPAQ, due to that reports are affected by state, beliefs and experiences.

It was observed that SPAQ, as an instrument to diagnose SAD, has a good specificity, but a low sensibility; in other words, SPAQ is not a sensitive instrument to detect accurately the criteria to diagnose SAD, but screens effectively seasonal symptoms. Michalak et al. (2001) found that 55% of the cases were false positives and just 0.4% met the criteria of SAD. The SPAQ is structured to detect seasonal changes in mood and behaviour, such as food intake, weight gain, sleep duration and sensitivity to environment (Mersch et al., 2004). The present study was limited to measure seasonal symptoms of physiological and psychological nature.

Figure 4. The risk and protective factors in the seasonal and depressive pyramid; risk factors follow a pathological continuum. The protective factors form a threshold that turns back the individual's metabolic balance.



2.4 Latitude and environmental variables related to seasonal variation

The environment is the principal factor that influences on health and mental well-being. Persons experience sadness, fatigue and lower performance in everyday life in winter time and milder symptoms during autumn or spring. The duration of daylight period in the winter, linked to latitude cultural and ethnical differences would also become important factors that influence on mood and energy (Magnusson et al., 2000; Tonello, 2001). Seasonal variations are present in persons diagnosed with SAD and in healthy ones as well (Mersch et al., 1999 b).

Several environmental variables have been suggested as important influences to the onset of seasonal symptoms: photoperiod (hours from sunrise to sunset) daily hours of sunshine, total radiation and mean daily temperature (Rosenthal et al., 1984 b). Photoperiod was suspected to be the principal environmental factor affecting mood and behaviour, due to its periodic function based on latitude and the days of the year. Its phase is set by the date in the calendar and the distance from the equator, which makes it shorter. Therefore, persons who live in higher latitudes experience earlier seasonal variations in cloudy and colder conditions (Young et al., 1997). These authors found that 74% of the individuals reported changes in the first week of November, the time when it gets darker earlier in the day. Total radiation, hours of sunshine and daily temperature were not relevant on the onset of seasonality, but might affect in its severity.

High latitudes were thought to be important factors for the onset of seasonal symptoms, as Partonen et al. (1993) tried to find out in a country located on 60-70 degrees north. Depressive symptoms in winter time did not correlate to latitude, but was prevalent in northern locations. Variables such as genetics, gender and race could be diverse in the photoperiod coding of serotonin transportation (Lurie et al., 2006). The sleep-wake cycle in women depended more on the daylight, so gender could be a key predictor of the variation of seasonal symptoms.

2.5 Association between seasonal and depressive symptoms

In wintertime, persons tend to report symptoms that bear a risk of a depressive episode. These symptoms do not have an accurate time to appear and suggest a pathological mechanism. First, Kasper et al. (1989 a) located persons with SAD on one side of the spectrum and persons without seasonal changes on the other side. So, in the middle could be persons with sub-SAD or SAD type symptoms (see figure 4). Young and co-workers proposed the dual vulnerability hypothesis in 1991, which consists in two groups of SAD symptoms: vegetative (fatigue, hypersomnia and increased appetite/weight) and affective, i.e. vulnerability to develop secondary depressive symptoms in the presence of stress of the winter energy, sleep and appetite symptoms.

The Dual Vulnerability Hypothesis was conceived as an interactional model to explain the aetiology of SAD. The individuals who have the symptoms of SAD based on the DSM-IV criteria for major depressive episodes have two vulnerabilities: seasonality in vegetative functions (sleep, appetite and energy/motivation) and affective and cognitive symptoms appear under stressful conditions, presented by changes in vegetative symptoms. Hypersomnia, hyperphagia and fatigue are risk factors that might be conducive to depressive symptoms, such as sad mood, decreased self-esteem, guilt and difficulty concentrating (Young, 1999; see figure 4). Seasonal symptoms such as sleep duration, appetite and energy level vary in the general population, but persons with SAD have remarked seasonal physiological symptoms and at the same time present cognitive, affective and behavioural symptoms associated with depression. Other individuals develop a winter anergia without depressive symptoms (Young et al., 1991).

Light and exercise are protective factors that prevent or treat vegetative symptoms as well as resynchronize circadian rhythms (see figure 4). Concerning the affective symptoms, both biological and psychological factors play a role in terms of vulnerability, onset, course, severity and treatment response. Therefore, it is important to study the interaction between vegetative and affective symptoms because it will lead to a better understanding of each entity separately and how they interact together in seasonality. Cognitive processes seem to be more sophisticated in higher organisms, especially in humans, and psychological processes are the consequence of their personal history of interaction with the environment. Vegetative symptoms are consistent manifestations of normal seasonal variation that are heritable, but cognitive and affective symptoms vary more from culture to culture (Young, 1999).

2.6 Metabolic phenomena in relation to seasonal variation in mood and behaviour

The metabolic syndrome is conceived as a group of metabolic disorders, such as impaired glucose metabolism, hypertension, dyslipidemia and abdominal obesity; which leads to diabetes type II and cardiovascular diseases (Tuomilehto, 2005). The definition that the WHO (WHO, 2000; Marchesini et al., 2004) provided was: impaired glucose tolerance, diabetes mellitus and/or insulin resistance together with two or more of the following: arterial blood pressure >140/90 mmHg; dyslipidemia defined as plasma triglyceride (TG) concentration >1.7 mmol/l (150 mg/dl) and/or high-density lipoprotein cholesterol (HDL-C) <0.9 mmol/l (35 mg/dl) in men, <1.0 mmol/l (39 mg/dl) in women; central obesity, defined as a waist-hip ratio (WHR) >0-90 in men, >0.85 in women and/or body-mass index (BMI) >30 kg/m^2, micro albuminuria, defined as urinary albumin excretion rate >20 mg/min or albumin:creatinine ratio >30 mg/g. According to the NCEP-ATPIII (Marchesini et al., 2004) defined it as: abdominal obesity, waist circumference of >102 cm in men and >88 cm in women; plasma TG > 1.69 mmol/l (150 mg/dl); HDL-C <1.03 mmol/l (40 mg/dl) in men, 1.29 mmol/l (50 mg/dl) in women; blood pressure >130/85 mmHg fasting glucose >6.1 mmol/l (110 mg/dl).

One of the consequences caused by obesity and a sedentary life is the prevalence of diabetes type II which is rapidly rising around the world. At the same time those persons with problems in their glucose metabolism are at risk for cardiovascular disorders. These subjects, especially men, had higher waist circumference, obesity, dyslipidemia, WHR, diastolic blood pressure, low density lipoprotein (LDL) cholesterol and triglycerides, but lower HDL cholesterol than the women. Both genders were found to have the same proportion of BMI>30 (Ilanne-Parikka et al., 2004).

These problems are caused by changes in lifestyle such as a diet high in saturated fats and a lack of physical exercise. Therefore, it is required to detect and treat persons with such syndrome to reduce its consequences in health by decreasing body weight and increasing physical activity (Tuomilehto, 2005). At the same time, the prevention of type II diabetes has to be a priority to prevent later vascular complications, not only improving glucose tolerance but also dealing with all the components of metabolic syndrome (Ilanne-Parikka et al., 2004). Therefore, it does not bring any benefit to store extra energy in lipid reserves in an environment with constant food supply (Bartness et al., 2002).

It was found that the metabolic patterns of the brain in patients with winter SAD had lower metabolic rate than persons without it; for example, they had asymmetrical (left more than right) metabolic activity of the medial prefrontal cortex. After they were treated with light therapy, their cerebral blood flow was increased in frontal and cingulated cortices and thalamus, in other words, they responded well to bright light therapy (Partonen and Lönnqvist, 1998).

Seasonal changes in adiposity are the result of the work of several hormones combined mediated by the photoperiod, so its actions cannot be explained by just a single hormone. Melatonin signals outflow through the sympathetic nervous system (SNS) modulating seasonal adiposity from the brain to the fat. So, the SCN is the main coordinator of seasonal changes because it works as a biological clock that generates circadian behavioural and physiological rhythms. The duration of night is the key environmental factor in decreasing body fat. At the pineal level this stimulus is translated into a biochemical signal through the duration of the melatonin secretion that follows the dark period (Bartness et al., 2002).

2.7 The effect of seasonal and depressive symptoms on quality of life

Persons with SAD suffer from depression in the autumn or winter with periods of hypomania or euthymia in the summer. Michalak and co-authors (2005) were interested to know if patients with SAD improved their perceived QoL during the summer months. They found out that QoL was better during the summer and improvements occurred in mental health, health perceptions and social functioning but not in physical functioning, role functioning and pain. Perceived QoL relating to emotional and social functioning is remarkably problematic in patients with SAD in the winter (Michalak et al., 2005).

Patients with this disorder reported markedly impaired QoL during the winter months, but light therapy improved their perceived QoL (Michalak et al., 2005). Their level of physical performance was acceptable, but mental health was impaired compared to the general population. Patients with non-seasonal depression scored poorly in many domains, such as physical, health perceptions and social functioning, but not in mental health function. QoL may present variations with marital status, education, income, race, geography and other psychological factors (Michalak et al., 2003).

Atypical depressive symptoms (carbohydrate craving, prolonged sleep, weight gain, increased appetite) come along with low indoors illumination as well as outdoors light exposure at high latitudes in wintertime. An adequate relief for these symptoms is training in bright light at a fitness level bringing high levels of vitality, improved general mental health and social functioning. Therefore, these interventions help to improve mood and some areas of health related quality of life during the winter (Partonen et al., 1998). It was reported in high latitudes problems in sleep, mood or energy depending on the season, in which women were more affected. Self-reported depression was low in winter due to the lack of daylight, but in summer, some minor sleeping problems were detected (Hansen et al., 1998). As Michalak et al. (2003) mentioned it is relevant to know how persons with seasonal symptoms perceive their QoL, so as to compare the level of impairment with other psychiatric problems and how to intervene with a planned treatment.

2.8 Architectural light and its influence on mood

The relation of the human being with his/her natural environment is given by a complex exchange of energy in different levels, starting with our body that responds to the variations of the environment by biological processes of adaptation. The natural energies present in the environment such as light, sound and heat interact in an architectural structure. As a consequence, human beings react in a physiological and psychological manner inside the habitat. Thanks to architecture it is possible to live under extreme weather conditions with revolutionary tendencies in technology and construction by controlling the energy, and the capacity to adaptation of the human beings to survive (Murguía, 2002; see figure 5).

Figure 5. The diversity of architecture is reflected by opposite weather conditions.

The human organism has developed homeostatic mechanisms that interact with the environment through the energy of adaptation. In order to keep a balance by this exchange of energy, biologists adopted a term called "Adaptation General Syndrome" (Murguía, 2002). Architectural spaces designed deficiently in terms of temperature, light and sound may cause health problems in persons; in other words the "Sick Building Syndrome" (Murguía, 2002). Individuals are very sensitive to changes in light from any source, so many of these biological, physiological and psychological effects seem to be moderated by the characteristics of these changes. It is relevant to put special attention to its intensity and distribution due to its additional effects indoors.

The role of artificial light is crucial due to the fact that its use has been intensified not just to facilitate sight but to influence in other biological aspects of human beings. Research studies carried out in optical physiology have been successfully applied in illumination technology. Czeisler and co-workers (1990) considered that modern artificial light is the principal responsible of circadian disruption in users. Natural light produces rapid and intense changes in the circadian clock, but the artificial light with less intensity can cause problems in the long-term by a lack of synchronization from 4 to 5 hours per day. Therefore, the opinion of many specialists is to implement preventive phototherapy in artificial light working spaces or offices. This therapy has the objective to be an active regulator of the circadian rhythms. Indoors lighting has been studied in laboratory settings so as to observe an impact on mood. It varies with the seasons and in different latitudes, so Küller et al. (2006) concluded that light and colour have an impact on persons' mood working in offices, especially in locations far from the equator. Workers' mood was rated as low when the environment was perceived either too dark or too bright. At the same time it might be relevant to choose adequate indoors colouring and to work next to a window. The authors suggested based on their results to study a healthy building, which is part of a complex system.

After reviewing these implications of artificial light on human health, the light designers have to plan new methods and strategies based on biological and medical research to improve indoors illumination. Murguía (2002) recommended the following aspects for future interventions: First, non-optical factors of light in human beings, by taking into account the geophysical variation of the environment as well as the circadian rhythms that control the physiological and psychological performance of the individuals. This is a relevant issue because it compromises the mood, level of stress and work performance. Second, energetic efficiency and environmental protection: fluorescent light and regulators together with an adequate design of the buildings that contemplate the entrance of natural light are beneficial to health and energetic saving for ecological purposes.

3 Aims of the study

The basic aim of this study was to assess the relation between the seasonal variations in mood and behaviour with various risk factors, such as gender, age and region of residence, and how they influence the intensity of the seasonal symptoms.

Other behavioural factors evaluated were the level of physical activity, alcohol intake and illumination received. The specific aims were described as follows:

I. Previous studies identified a seasonal pattern in mood disorders (depressive and bipolar disorders). The seasonal changes in mood and behaviour and the intensity of depressive symptoms was assessed in the Finnish general population. The question in this study was: *Are seasonal and depressive symptoms associated?*

II. Metabolic syndrome is considered as a frame of disorders that produces high risk factors on health. It was reported whether seasonal changes are a risk factor to develop metabolic syndrome, originated by abnormalities in the circadian rhythm. The question for this study was: *Can seasonal variations increase the risk of metabolic syndrome?*

III. Seasonal variation in appetite and weight as well as poor indoors illumination were used as predisposing factors, and studied whether these three affected the report of changes in mental health by season among Finns aged 30 or over. In addition, physical exercise and alcohol intake were assessed as behavioural indicators. The questions for this study were: *Are seasonal variations in appetite and weight indicators of metabolic syndrome? Do physical exercise and alcohol intake influence on these seasonal variations?*

IV. Seasonal variations in mood and behaviour, as well as insufficient illumination at home and at work, might decrease the quality of life and mental well-being. It was assessed a possible relation among these variables. The questions in this study were: *Are seasonal variations in mood and behaviour related to a decrease in the quality of life as well as mental well-being? Can poor illumination at home and at work affect mental well-being and quality of life?*

4 Material and methods

4.1 Sample

An epidemiological survey called The Health 2000 Study started at the end of the summer of 2000 and concluded at the beginning of the spring of 2001 in Finland. Data was collected from 8028 adults aged 30 and over (55% women) who participated, in five university hospital districts with one million inhabitants in each one of them (see table 1). They were classified according to their demographic characteristics, sampling 15 biggest cities and 65 areas using the probability proportional to population size method. Afterwards, the subjects were randomized using the data given by the Population Register Centre. The resources used to collect data were by face-to-face interview at home as well as an individual health status examination. A series of questionnaires were provided to be returned at the time of their health status examination. Additionally, the participants received another set of questionnaires to post back together with venous blood samples for laboratory tests.

Further information is described in http://www.terveys2000.fi/indexe.html.

Table 1. Descriptive characteristics of the Finnish Health 2000 Study sample by age and gender.

AGE	MEN	WOMEN	TOTAL
30-34	415	441	856
35-39	449	470	919
40-44	452	442	894
45-49	462	495	957
50-54	501	462	963
55-59	319	346	665
60-64	293	324	617
65-69	229	272	501
70-74	193	299	492
75-79	118	228	346
80-84	126	326	428
85-89	60	208	268
90-94	17	69	86
95-99	3	9	12
TOTAL	**3637**	**4391**	**8028**

4.2 Assessments

Descriptive variables were classified by the gender, age (categorized from 30 to 45, 46 to 60, 61 to 75 or 76 to 99 years), residence (the northern or southern part of Finland), education (categorized as low, medium and high), marital status (living alone or with someone), physical exercise categorized as low (no strenuous exercise, such as reading, watching television or handicraft), medium (lightly strenuous exercise, such as walking or bicycling for four or more times a week), keep-fit (fitness training for three or more hours a week) or sport (sports activities for several times a week), and alcohol intake (in categories of low, medium, high or none) were entered as independent explanatory variables.

4.2.1 Depressive and seasonal symptoms

The Beck Depression Inventory (BDI) was completed by 6311 Finnish individuals. It is composed by 21 items each with four possible responses that measure depressive symptoms and signs, with a sum score from 0 to 55. Each response ranges from zero to three marking the severity of each symptom. Its aims were to assess the presence and the severity of depressive symptoms of individuals aged 13 and over, without being used for diagnostic purposes (Beck and Steer, 1984). Each question assessed mood, pessimism, sense of failure, self-dissatisfaction, guilt, punishment, self-dislike, self-accusation, suicidal ideas, crying, irritability, social withdrawal, body image, work difficulties, insomnia, fatigue, appetite, weight loss, bodily preoccupation and loss of libido. Items 1 to 13 assess psychological symptoms, and 14 to 21 items assess physiological symptoms (Beck et al., 1961; Polgar, 2003).

The Seasonal Pattern Assessment Questionnaire (SPAQ) (Rosenthal et al., 1984 a) was answered by 5953 Finns and 5749 filled them both SPAQ and BDI. SPAQ measured the seasonal variations in mood and behaviour, using the Global Seasonality Score (GSS) with punctuation from 0 to 18. The reliability of the GSS was confirmed by test-retest (Magnusson, 1996; Magnusson and Friis, 1997).

Apart from the six items, it was important to consider if the symptoms were problematic (no, mild, moderate, severe) to the individuals. The cut-off for the SPAQ was between 7 and 8 (not affected versus affected).

4.2.2 Diagnosis

The mental health interview was performed at the end of the comprehensive health examination. In this study, the Finnish translation of the German (Munich), computerized version of Composite International Diagnostic Interview (M-CIDI) was used (Pirkola et al., 2005). The program used operationalization to meet the DSM-IV criteria and allows the estimation of DSM-IV diagnoses for major disorders. The translation of the M-CIDI was made pair-wise by psychiatric professionals and revised by others. The official Finnish translation of the DSM-IV classification was used as a basis for formulating the interview. The process included consensus meetings, third expert opinions, an authorized translator's review, and testing with both informed test subjects and unselected real subjects.

A team of 21 non-psychiatric professionals in the health care field were trained for the M-CIDI interview during 3-4 days by psychiatrists trained by a WHO authorized trainer. The translation of the M-CIDI was carried out and revised by psychiatric professionals. In order to formulate the interview, the official Finnish translation of the DSM-IV classification was consulted. The duration of the interview was 23 minutes in average (Pirkola et al., 2005). Interviews were performed to determine the 12-month prevalence rates of major depressive episodes and disorder, dysthymia, general anxiety disorder, panic disorder with or without agoraphobia, social phobia, alcohol abuse and dependence, and other substance dependence and abuse. These were grouped into categories of depressive, anxiety and alcohol use disorders. Comorbidity was defined as persons having suffered from any of these disorders from more than one category within the last 12 months (Pirkola et al., 2005).

The test-retest reliability of the depressive disorders section in the interview was examined by 49 visitors in occupational health services. The Kappa values reported in the interviews were 0.88 (95% CI of 0.64-1.0, observer agreement 94%) for major depressive disorder, and 0.88 (95% CI of 0.64-1.0, observer agreement 98%) for dysthymia (Pirkola et al., 2005).

4.2.3 Laboratory tests

Several laboratory tests were applied such as total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, urate, gamma-glutamyl transferase, and of blood glucose. In addition, height and weight were taken to calculate the body-mass index as well as the waist circumference.

4.2.4 Metabolic syndrome

Metabolic Syndrome was assessed by using the US Adult Treatment Panel III of the National Cholesterol Education Program (NCEP-ATPIII). Individuals need to have at least three symptoms: fasting blood glucose level of 6.1 mmol/l or higher, high blood pressure (systolic pressure was 130 mmHg or more or diastolic pressure was 85 mmHg or more), serum triglycerides level of 1.7 mmol/l or higher, serum high-density lipoprotein cholesterol level lower than 1.0 mmol/l for men or lower than 1.3 mmol/l for women and waist circumference of 102.1 cm or more for men or 88.1 cm or more for women.

4.2.5 Health-related quality of life

Health related quality of life (HRQoL) measures the individual’s ability to perform in life and attitude towards well-being in physical, mental and social activities. It evaluates basic activities such as self-care (e.g. bathing, dressing), work-related activities and the ability to interact with family and friends. In addition, it considers if the individual feels happy, sad, depressed or anxious, if they are in pain or not, energetic or lethargic (Hays and Morales, 2001).

The HRQoL was assessed with the 15D health-related quality of life instrument (15D) that measures breathing, mental function, speech, vision, mobility, usual activities, vitality, hearing, eating, elimination, sleeping, distress, discomfort and symptoms, sexual activity and depression (Sintonen, 2001).

4.2.6 Mental well-being

The General Health Questionnaire (GHQ-12) evaluates the current mental health (Goldberg and Hillier, 1979) applied in different settings and cultures. The original questionnaire has 60 items, but was shortened to 12 items. It considers recent symptoms or behaviours categorized in four alternatives (less than usual, no more than usual, rather more than usual, or much more than usual). The latest version is brief and easy, which makes it a useful screening tool for documentation purposes (Montazeri et al., 2003).

4.2.7 Experienced illumination

The self-perception of illumination at home and at work was estimated with questions and their answering options were: Poor lighting at home? (Yes/No). Insufficient lighting at work? (No present/no problem/troubles to some extent/troubles quite much/troubles a lot).

4.2.8 Physical activity and alcohol use

As part of the assessment, the participants filled in items concerning leisure time exercise habits and use of alcohol during the past 12 months. The intensity of exercise habits was categorized as follows: low (no strenuous exercise, such as reading, watching television or handicraft), medium (lightly strenuous exercise, such as walking or bicycling for four or more times a week), keep-fit (fitness training for three or more hours a week) and sport (sports for several times a week). The frequency of alcohol use was categorized as follows: none, low (once to six times a year), medium (once to four times a month) and high (twice to seven times a week).

4.3 Ethics

The National Public Health Institute organized this project in collaboration with the Ministry of Social Affairs and Health. Each participant received a written consent and the protocol was fully described to them. Everything covered the requirements of the ethical standards of the responsible committee on human experimentation as well as the Declaration of Helsinki.

4.4 Statistics

The R project for Statistical Computing (R, version 2.2.1) was used in the analysis of data that come from a survey stratified, cluster-sampled and unequally weighted, or complex, survey design using survey-weighted generalized linear models. The advantage of this programme is that it can produce symbols and formulas, if required. Further benefits are: a) It can handle data effectively, b) It calculates matrices, c) It provides tools for data analysis as well as graphics, d) It has an effective language with conditionals, loops, and other facilities.

Coefficient analysis was used to calculate associations followed by chi-squared tests. Two binomial logistic regression models were formulated to control confounding factors, such as gender and age. Sampling design was weighted to reduce bias and correct over-sampling of the elderly.

5 Results

5.1 Basic findings

The basic findings in this study were that 85% of the Finnish population presented seasonal variations in mood and behaviour and 2.6% had symptoms that corresponded to SAD (see figure 6). The principal factors that contributed to seasonal variations were depressive symptoms, being female (OR=1.85, 95% CI of 1.48-2.32) and ages between 60 and 75 (OR=0.70, 95% CI of 0.50-0.99). Neither the global seasonality score nor the BDI sum score was associated with latitude. Increased sleep was reported more frequent in northern regions.

The explanatory variables of seasonal variations and metabolic syndrome were old age, depressive symptoms (BDI), seasonal symptoms (GSS) and northern latitude residence (study I). In addition, poor indoors illumination, seasonal variation in weight and appetite contributed to this problem (study IV).

Indoors illumination and seasonal symptoms were factors that affected on HRQoL and mental well-being. Low energy level (t=-4.26, P<0.001), low mood (t=-3.62, P=0.0031) and low social activity (t=-2.18, P=0.029) were significant contributors in HRQoL. Concerning mental well-being, low mood (t= 2.77, P=0.0057), increased appetite (t=2.54, P=0.011), low social activity (t=2.21, P=0.027) and energy level (t=2.11, P=0.035) were relevant explanatory variables.

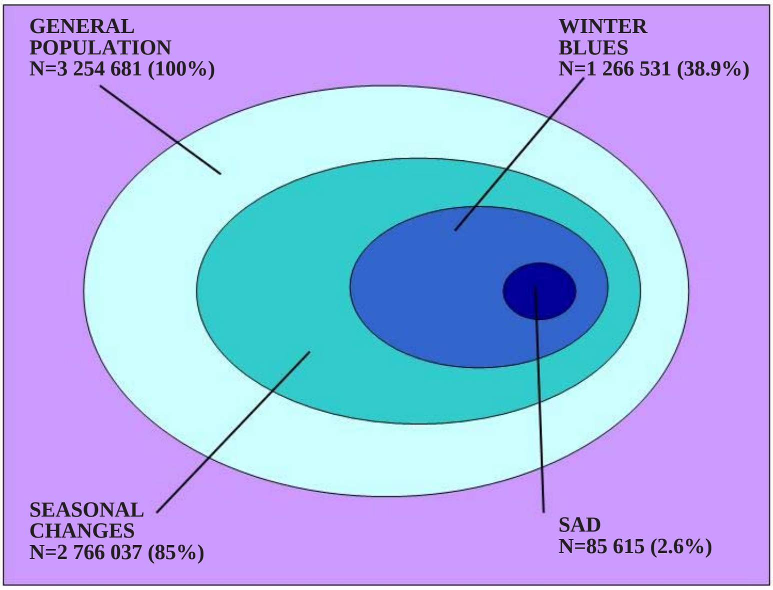
5.2 Associations between seasonal and depressive symptoms (I)

GSS and BDI combinations were created and found that the presence of seasonal symptoms and depression was 9.1%, 17.8% with high BDI and low GSS, 11.1% high GSS with low BDI, and 62% of the sample had a low score in both scores (see figures 6 and 7). 38.9% of the individuals experienced mild symptoms, 15.3% moderate and 3% severe and disabling. 11% did not report seasonal changes and 0.3% had a high GSS.

When high/low scores in GSS and BDI were organized subjects in group two (high GSS and low BDI) had changes in sleep length with 10.4%, compared to group three with 8.5% (high scores in both scales). Social activity, mood and energy with 10.5%, weight 9.4%, and appetite 9.3% were for group two, and for group three there were changes in social activity with 8.4% as well as mood and energy with 8.6%, weight 7.3% and appetite 7.6%.

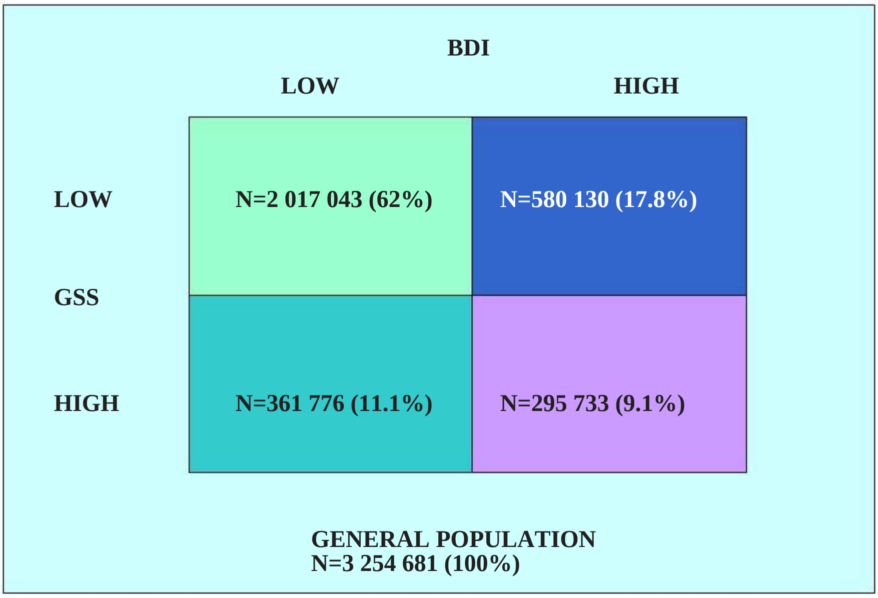
A significant correlation between GSS and BDI was obtained with r=0.31 and P<0.001. The regression models showed that higher scores on the SPAQ were significantly associated with depression as well (OR=3.05, 95% CI of 2.63-3.53) and higher scores on the BDI with the seasonal pattern (OR=3.05, 95% CI of 2.63-3.53).

Figure 6. Prevalence of seasonality, winter blues and SAD in the Finnish population.



Abbreviation: SAD = Seasonal affective disorder.

Figure 7. Seasonal and depressive symptoms in the general population.



Abbreviations: BDI = Beck Depression Inventory; GSS = Global Seasonality Score.

5.3 Seasonal variations in weight and appetite predispose to the metabolic syndrome (II, III)

High scores obtained by subjects with seasonal changes in weight and appetite increased the risk of metabolic syndrome in 53% of the cases. Nevertheless, other explanatory variables such as female gender, poor lighting at home, higher scores on self-reports of mental well-being or depressive symptoms, bigger waist or pelvic circumferences and major depressive disorder were experienced as problematic by 89% of them. These results suggest the influence of circadian cycles over metabolism and mood, in which a shorter photoperiod as well as poor indoors illumination lead to seasonal changes in appetite and weight.

Physical exercise was a useful protective factor to decrease GSS score, especially for those that trained at a fitness level. It was useful especially for the ones who experienced seasonal changes, and their problem was reduced by 25%. A key factor in seasonality is the decrease in physical activity and the increase in the rest metabolic rate. Other factors that influenced on the intensity of the seasonal changes in mood and behaviour were the BDI sum score, gender, education, pelvic circumference and the GHQ-12 sum score. Indeed, depression, anxiety and alcohol use disorder made a more intensive experience of seasonal changes at the beginning of the autumn. Individuals that suffered more from depression presented more seasonal symptoms such as sleep length, weight and appetite. On the other hand, persons with anxiety had seasonal changes in social activity.

The variation of the GSS could be explained in 53% with weight and appetite, and 89% with sleep length, social activity, mood and energy level. The seasonal symptoms that contributed most to metabolic problem were weight and appetite. It was found in the Finnish population that 49.5% have seasonal changes in weight and 42.4% in appetite. From those individuals diagnosed with metabolic syndrome, 56.1% and 46.6% presented seasonal changes in their weight and appetite. The signals related to metabolic factor were female gender, poor lighting indoors at home and bigger waist circumference.

The prevalence of metabolic syndrome was higher in individuals with high GSS (z=2.8, P=0.05) (r= 0.07, P<0.001). The most common symptoms were appetite (r=0.07, P<0.001), weight (r=0.10, P<0.001), mood (r=0.34, P=0.01), length of sleep (r=0.04, P=0.003), and energy level (r=0.37, P=0.005). When the risk level was calculated, weight was an important factor (OR=1.43, 95% CI of 1.23-1.60, SD=0.06), caused by changes in appetite (OR=0.1, 95% CI of 0.87-1.13, SD=0.07), changes in length of sleep (OR=1.07, 95% CI of 0.97-1.18, SD=0.05), in energy level (OR=1.02, 95% CI of 0.92-1.15, SD=0.06) and in mood (OR= 1.02, 95% CI of 0.93-1.13, SD=0.05).

Other risk factors were age, gender with prominent prevalence in men and living in the north. However, persons with high education and an adequate level of physical exercise decreased the risk to develop metabolic syndrome. Metabolic symptoms with significant difference were BMI (t=-42.7, df=3513 P<0.001), waist circumference (t=-47.2, df=6560, P<0,001), and plasma glucose levels (t=-19.2, df=2339, P<0.001). It was also observed higher plasma levels of total cholesterol (t=-13.2, df=6631, P<0.001), HDL-cholesterol (t=48.5, df=5452, P<0.001), LDL-cholesterol (t=-11.9, df=3800, P<0.001) and triglycerides (t=-37.5, df=2468, P<0.001). Surprisingly, gamma-glutamyl transferase values were higher in individuals with metabolic syndrome, despite their decreased use of alcohol (t=10.2, df=2975, P<0.001). Urate levels were higher in them (t=-26.6, df=3659, P<0.001), and their level of exercise was less (t=11.7, df=6445, P<0.001).

5.4 Associations between seasonal variation and experienced illumination (III, IV)

A high GSS score was an important factor to evaluate the influence low illumination has at home (0.5%), at work (3.2%), either of them (17.4%), and both of them (0.53%). Therefore, it was suspected the lack of an adequate illumination increases seasonal symptoms. There were some differences in gender and age. Men between 30-45 years with seasonal changes reported more frequently low illumination at work (5.2%), but for 69.2% of them it was not a problem, even if it was low at home as well (54%). Some individuals had problems to sleep (78%), to socialize (75%), in mood (80%), in appetite (63.6% and 42.6%), weight (64.7% and 48%) and energy (85.2% and 78.4%) when illumination was low at home and at work.

5.5 Seasonal variation and illumination in relation to health related quality of life (IV)

The quality of life factors that were more affected by seasonal symptoms were movement (78.9%), hearing (83.7%), breathing and mental (67.3% and 68.7%), eating and speech (98.2% and 91.4%), elimination, mental and sexual (63.5%, 65.5% and 63.9%). High scores in GSS reflected problems in sleeping (34.4%), vitality (31.3%), depression (46.9%) and discomfort (28.2%).

5.6 Seasonal variation and illumination in relation to mental well-being (IV)

Some symptoms that were common among those having a high GSS were difficulties to face problems (21.6%), problems in concentration (27.7%), overcoming difficulties (22.9%), sleep disturbances (28.5%), enjoying daily activities (28.5%), loss of confidence (21.7%) and lack of happiness (22.6%).

6 Discussion

6.1 Seasonal variations and latitude (I)

Seasonal variations in mood and behaviour were present in 85% of Finns, 9% had both seasonal and non-seasonal symptoms of depression and 2.6% of possible cases of seasonal affective disorder. These percentages show that seasonal symptoms are common and relevant on the health status of a population. So, adaptation to a Nordic environment is essential on the regulation of mood and behaviour (Saarijärvi et al., 1999; Magnusson et al., 2000).

Individuals with a higher GSS suffered more from depressive symptoms, especially older women with seasonal variations in mood, appetite, energy level and social activity. The principal question would be the factors that trigger them. Blazer and co-workers (1998) mentioned that men and older age persons present a high seasonal pattern with major depression. No relation between age and seasonal variations was found in this study herein. Concerning women, the action of estrogen (Kruijver and Swab, 2002; Cai et al., 2008) and sleep length (Kronholm et al., 2008) provide a feedback on the SCN Terman et al. (2008) detected a large number of winter depression cases in different locations in the United States. Time zones had a significant effect on seasonal variation rather than latitude above 38°N. This study contradicts such findings with no significant effect on mood and behaviour except sleep duration in the Finnish population, which follows a different lifestyle and migratory frequency compared to the United States (Mersch et al., 1999 a).

Latitude, coastal and inland weather region are indirect indicators of daylight during the winter, which means that later sunrise times affect on sleep length. Other factors such as physical exercise, higher education, marital status, social activity and alcohol use affected seasonal variations reports and may have a more powerful effect on their incidence than high latitude or short photoperiod. Preventive measures in physical training and alcohol misuse should be applied to improve well-being. At the same time it is required to have a deeper comprehension of the mechanisms of action behind seasonal variations in mood and behaviour and their regulation, to make a more accurate diagnoses and give an integral view of mood disorders.

6.2 The dual vulnerability hypothesis

Seasonal symptoms such as length of sleep, appetite and energy level have seasonal variations in the general population and vary within individuals. Young (1999) defined the dual vulnerability hypothesis as a model of interaction to understand the origins of SAD with two vulnerabilities: 1) Tendency to develop vegetative symptoms, such as sleep, appetite and energy/motivation. 2) Tendency to develop affective and cognitive symptoms in response to a stressful life. Such stress is due to changes in vegetative functions (metabolism). Persons who experience such condition have a higher risk to develop SAD, depending how they interact with the environment. The duality was described as follows: a) Individuals with only the psychological vulnerability are depressive. b) Individuals with only vegetative vulnerability are sub-SAD. c) Individuals with both symptoms are SAD. Thus, the duration of the symptoms, irritability and the capacity of self-regulation are relevant factors to take into account to develop vulnerability.

When external conditions start to change, vegetative symptoms appear as an adaptive adjustment. The "open systems theory" developed by von Bertalanffy (1950) made emphasis on the importance of chemical and physical (thermodynamic) components to maintain the organism in a constant regulation. The first problem encountered with this theory was that it did not describe which chemical and physical processes regulate metabolism to keep an adequate homeostasis. The model of open system stipulated that, first, organisms experience a great deal of chemical, physical processes and high energetic consumption (degeneration and regeneration) that allow a living cycle as well as the capacity of doing work. Even the resting cell, not performing "activity", needs a continuous energy supply for living (conservation of energy). Second, they are continuously exchanging matter within the environment (external conditions) and respond to external stimuli, by a disturbance and re-establishment of a steady state (adaptation). Third, they try to maintain a constant blood temperature (thermodynamics). Fourth, the metabolism differs under basal conditions of muscular activity as well as in different seasons of the year. Fifth, chemical equilibrium is based upon reversible reactions. Steady states are irreversible as a whole and individual reactions concerned may be irreversible as well, so as the system maintains a steady state. This author conceived human beings as "open systems" that constantly interact with their environment. The psycho-physiological activities have a homeostatic principle. A living organism can respond to a stimulus, recover its internal balance to adjust to the environmental changes.

According to the "open systems theory", the organism tries to keep a balance between chemical and thermodynamic states. Such balance is reflected in metabolism changes and muscular activity along seasons. For instance, patients with SAD report increased activation following high-carbohydrate meals in winter time. SAD subjects reported to react to stressful situation with greater emotion and depression. The ones with high anxiety are more likely to monitor their physiological state as well as to believe that their symptoms will have negative outcomes (Lam et al., 2000). It means that the greater their emotional response to stress is, the earlier the depressive symptoms appear in winter. The factors that contribute are personality, sensitivity, reactivity, rumination and amplification of moods. In SAD, cognitive-affective symptoms are developed and vegetative symptoms are intensified (Young, 1999).

Individuals having sub-SAD and SAD differ in their exposure to depressive (stressful) life events and probably by their genetic factors. Photoperiod is the principal factor that initiates vegetative symptoms in SAD (Lam et al., 2000). However, temperature plays an important role when considering carbohydrate craving and gaining weight. Concerning the genetic factor, it can play a role either as a risk or protective factor, and may vary between males and females (Lam et al., 2000). For instance, women with a gene that codes for a serotonin receptor have alterations in serotonin function as well as attention deficit disorder (Lurie et al., 2006).

The dual vulnerability hypothesis claims that there are factors of seasonality and that of depression in SAD. It includes phase-shifted circadian rhythms, serotonergic dysfunction and genetic vulnerability. The question would be whether or not it is a dimension of diagnosis of SAD. According to Lam et al. (2000) it possesses dimensional characteristic rather than following a pattern. Not all the individuals experience SAD symptoms at the same time. When there are changes in the environment, their system starts to present vegetative symptoms (metabolic changes), and irritability might appear later. The manner in which persons deal with irritability depends on a threshold that would help them to recover their balance; two key factors have to be observed: 1) Metabolic changes present problems to the individual, especially to women who are more sensitive and can develop depressive symptoms. The more sensitive (affectively) they are, the more irritable, impulsive and depressed can become. 2) Women with impulsive tendencies score higher in seasonality, which might explain the carbohydrate craving behaviour as well. Therefore, those women fail to recover their balance and start to develop depressive symptoms. They do not have a threshold, but might follow a continuum in SAD pattern (Young, 1999).

Another characteristic that increases the risk of vulnerability is the "locus of control" proposed by Rotter (1954) or self-control. Locus of control means the capacity of the people to acquire control over their lives in case of stress or dramatic changes. Individuals that make choices to change their lives are considered to have internal locus of control. On the other hand, the ones to feel that environment has a powerful effect on them have an external locus of control. Therefore, persons with an external locus of control have higher risk to develop SAD and/or depression. SAD sufferers had a more external locus of control, consistent on a strong seasonal component of their experience.

If the individual has a genetic protector as well as an internal locus of control that allows him/her to recover the balance in case of irritation, he/she does not follow a SAD continuum, and higher levels of tolerance appear as a consequence (Murray, 2003)

6.3 Seasonal variations and illumination contribute to the metabolic syndrome (II, III)

Seasonal variations in mood and behaviour, specifically in weight and appetite as well as poor indoors illumination were significant risk factors that contributed to metabolic syndrome. Other risk factors related were increased waist circumference, female gender, older age, non-seasonal depressive symptoms, and living in the northern region. These associations indicate a strong link between human genetics and environment. Depression, anxiety and alcohol use disorder were diagnostic conditions that influenced on seasonal variations experienced as problematic. On the other hand, physical exercise and social activity were significant protective factors against metabolic syndrome.

This study confirmed that individuals with seasonal changes in mood and behaviour have a higher risk to suffer from metabolic syndrome. Adults were the most vulnerable group due to the fact that once they gain about half a kilogram in the autumn, their weight becomes accumulative every year and do not lose it during the spring or summer time as described in Yanovski and co-workers (2000) research. However, increasing the level of physical exercise to a fitness level can prevent weight gain.

An estimation of the circadian clock function can be obtained by assessing seasonal variations in mood and behaviour due to its plastic property (Scheer et al., 2007). It coordinates metabolism and controls rest-activity cycles, which can be more elastic in seasonal individuals (Teicher et al., 1997; Abrahamson and Moore, 2006; Sakurai, 2007).

The metabolic and circadian cycles are linked to affect on mood. It remains unknown the role of circadian rhythm in seasonal variations and metabolic syndrome, but alternative theories have been developed to explain it. Circadian, sleep-wake and seasonal cycles may be related in the intrinsic function of the metabolic cycle so as to preserve a healthy cell division (Tu and McKnight, 2006). On the other hand, day-night transitions as well as artificial light exposure are the principal basis to reset the principal circadian rhythm. A shortening in photoperiod at the beginning of the autumn reduces physical activity and might produce seasonal variation in appetite and weight (Zambon et al., 2003). When organisms are lacking of environmental signals, their biological clock presents delays and has to rely on metabolic signals from the peripheral organs (Zhang et al., 2006; van Oort et al., 2007). Therefore, programmed exposures to light may help to reorganize circadian rhythms (Thompson et al., 1997).

6.4 Seasonal variation and the metabolic syndrome are a window to the circadian clockwork

Human performance is not uniform along the day, but presents a clear circadian pattern known as sleep-wake cycle composed by 16 hours of high activity (energetic exchange, body temperature, hormone production, brain waves, muscular tone, etc.) and 8 hours of low activity (REM sleep). Cognitive functions such as memory, concentration, attention, time of reaction, manual activities and alert state are influenced by this cycle. Intellectual performance decreases during the night as well as physiological functions such as temperature regulation. The circadian rhythms are regulated by the amount of light received by the organism, which influences not just our daily activities, but behaviour as well. Disturbances in daily circadian patterns are reflected in lack of appetite, low mood and depressive episodes (Partonen and Lönnqvist, 1998).

Mood disorders are a consequence of a malfunction originated by the psychobiologic rhythms (circadian rhythm) (Orsucci, 2006). There is a possible relation between the circadian rhythms and depression, due to the fact that these rhythms help the living beings to synchronize their activities with temporal fluctuations in the environment. The light-dark periods as well as social and physical activity regulate the SCN functions. Melatonin sends information to the body clock during the day/night and is responsible to control the body temperature. When there is a disorder in the melatonin secretion pattern, specifically with lower concentrations, it can cause SAD, Bibolar disorder, bulimia, etc. Seasonal affective disorder is an example of how circadian rhythms are delayed with the environment and with other rhythms such as sleep-wake cycle. Patients with this disorder also have delayed melatonin rhythms that can be corrected with bright light therapy in the mornings to advance physiological rhythms. (Lam and Levitan, 2000).

Physiological processes in living beings are coordinated by circadian rhythm fluids from molecular to cellular and systems. Molecular biology has reached a deeper knowledge of the genetic and cellular dynamic world of metabolism. Cell cyclic division needs from other internal agents that generate and coordinate the process, such as protein consumption, sleep and wakening activity. A correct cellular division allows a faithful replication of genetic information contained in DNA. Substances called metabolites circulate over the circadian rhythms to control the functions of the proteins (Tu and McKnight, 2006). Light intensity seems to determine metabolic work, causing changes in circadian rhythms. Therefore, metabolism seems to coordinate circadian rhythms, including sleeping.

Sleep is an important activity in a 24 hr cycle due to its restorative properties in the living body to keep an adequate homeostasis. Sleep homeostasis is related either to restoration or loss of brain's function and store (Gillete and Sejnowski, 2005). Sleep has the function of resting, recharging and detoxifying the brain after the metabolic activity in waking times. In order to keep a regular cellular activity when neurons are in action, the organisms have to satisfy their metabolic requirements in waking times. Therefore, metabolism would be the key in homeostasis and sleep (Tu and McKnight, 2006). The slow wave sleep helps to adapt to environmental stress and when this sleep stage is incomplete by deprivation, stress and deficiencies in memory appear as a result (Maquet et al., 1997). The origin of circadian and sleep-wake cycles, the relationship between homeostasis and sleep, and the function of sleep in metabolic processes (e.g. energy conservation, thermoregulation, adaptation to the environment, restoration of tissues, memory process, etc.), remain unclear.

Biological systems have to adapt to longer periods of time, so seasonal variations appear in metabolic and behavioural activities dominated by light and food availability in the environment. Food is the most important resource to set biological rhythms and organisms that live in northern latitudes have to compete harder for nutrients in shorter light-dark periods, which make them more exposed to light stress. In spite of the complexity and organization of physiological and developmental systems in mammals during the day/night cycle, there could be evidence of the ancestral response to changes in the environments (e.g. temperature) for their regulation (e.g. increased appetite) (Gillete and Sejnowski, 2005). Circadian rhythms let them synchronize their metabolism depending on the day-night periods. Studies done in genome-wide expression reported that the circadian rhythms manage the time expression in metabolic genes. It is unknown the relationship between metabolism and circadian rhythm (Tu and McKnight, 2006).

SAD is associated with serotonergic malfunction and possibly with noradrenergic mechanisms. It may be also related to attention-deficit/hyperactivity disorder. Both conditions are disorders of the central nervous system with a heightened sensitivity to stimuli from the physical environment (Lurie et al., 2006). Tryptophan-depletion shows that serotonin is an important component in SAD and non-seasonal depression. The highest levels of this enzyme were have been found in April and May, but decreased in the late summer/early fall. Higher plasma levels of free tryptophan were also in the spring with lower levels in both early summer and winter periods. Indeed, seasonal people might be in a state of chronic under-arousal mediated by low dopamine activity in fall/winter months (Lam et al., 2000).

After analyzing the epidemiological data based on the Finnish population allowed it was concluded that changes in the environment, especially in light make persons more seasonal and depressed. Appetite and carbohydrate craving increase, if fitness training is not part of a daily programme, may cause waist circumference increase and a risk to develop metabolic syndrome. Therefore, their quality of life and mental well-being suffer.

Poor indoors illumination and shorter periods of sunlight in the autumn lower the stimulation of the SCN, which contributes to seasonal changes in appetite and weight. Factors that contribute to the seasonal symptoms are waist circumference and female gender, which suggest a genetic and environmental connection.

Architects can manipulate artificial light with advanced housing design for health promotion purposes. Intelligent housing solutions using computer-driven operations for the design of lighting levels and schedules during the day may be of benefit to individuals or groups having seasonal changes in mood and behaviour, or those who experience these changes as a problem. SAD provides the strongest evidence to identify a link between circadian rhythms and depressive disorder, when presenting phase delays. These delayed rhythms are also related to other disorders such as bipolar and night compulsive eating disorder. Interventions such as light, melatonin pills or sleep deprivation are useful to correct abnormalities in daily rhythms as well as neurodegenerative disorders such as Alzheimer’s disease. Therefore "the circadian model is clearly beginning to bear fruit... It is logically getting extended beyond SAD and should lead to better treatments for a number of psychiatric disorders" (Bhattacharjee, 2007).

These are explained by the morning hours that stimulate the SCN to accelerate its activity and avoid physiological delays. On the other hand, variations in light-dark transitions produce elasticity in the rest-activity cycles without resetting the SCN daily activity, so it relies more in metabolic activities for adaptation.

6.5 Seasonal variation as a biological principle to keep a homeostasis

An advantage that animals have to keep their homeostasis in colder and darker periods is their brown adipose tissue for thermoregulation purposes; a product of natural selection to favour adaptation in response to the coming season. Obesity was suggested as a metabolically efficient mechanism to keep energy as body fat. However, increased weight in humans does not seem a survival strategy due to its consequences to health. Therefore, animal are more efficient by regulating their body fat levels with changes in the season. Species exhibiting seasonal adiposity can be divided into three; Seasonal variations in the first ones vary with photoperiod, the second ones with circadian rhythms and the third ones respond with both changes and their fat level is easily regulated, compared to humans. Perhaps, humans with deficiencies in their physiological self-regulation and adaptation to new situations might develop psychopathological problems as a result of a dysfunction in their system. Therefore, irritability and other mental symptoms might appear as a continuum of a pathological process (Young, 1999; Bartness et al., 2002).

Increased appetite and weight as seasonal changes are important metabolic factors which may lead to metabolic syndrome. A deep link between metabolism and circadian rhythms would be related to seasonal changes in mood. Women living in low indoors illumination and having a big waist circumference are predisposed to such changes and to experience them as problematic; estrogen activity and/or sleep duration may provide a feedback on the SCN. Shorter light exposures at the beginning of the autumn induce to carbohydrate craving and a longer sleep due to the lack of stimulation of the principal circadian regulator (SCN). Circadian activities such as rest-sleep and fasting-eating are naturally flexible and dependent on light-dark transitions. However, if light exposures are continuously altered, these will carry abnormal cell division and other physiological and behavioural processes.

Circadian rhythms regulate the physiological rhythms in every living organism. These are essential systems that measure the time, anticipate to environmental changes and adapt through different times of the day. Any disorder in this clock might influence on human health due to the fact that biological rhythms and metabolism are in constant interaction so as to keep a regular and healthy cellular activity. The results of this study give support to the relations among metabolic, circadian and seasonal cycles generated and guided by the SCN. The link between circadian rhythms and cellular energy can contribute to the patterns followed by the organism during day and night. These findings would allow the creation of new treatments against cancer, diabetes, obesity, premature aging as well as prevent depression and other mood disorders (Grimaldi et al., 2009).

6.6 Seasonal variation and illumination affect HRQoL and mental well-being (IV)

The seasonal variations in mood, energy level and social activity together with experienced poor indoors illumination contributed to decrease HRQoL and mental well-being. A shortage of light exposure during the daytime increases seasonal variations and decreases HRQoL and mental well-being. Such effects became worse depending on the gender, age and education of the individuals. A major depressive episode might affect QoL, too. In order to improve mental well-being, outdoors and social activities have to be practiced regularly. Nevertheless, if a major depressive episode appears, the QoL would decrease even though having an adequate physical level (Michalak et al., 2004).

A scheduled bright light indoors exposure during the autumn and winter might increase the level of vitality, quality of sleep, physical activity, energy level and social activities, and at the same time decrease the intensity of depressive symptoms (McColl et al., 2001). Physical activity decreases depressive symptoms (Partonen et al., 1998), and bright light decreases seasonal variations in appetite, carbohydrate craving and prolonged sleep (Leppämäki et al., 2002). Architectural light has the capacity to manipulate indoors illumination at different levels and schedules during the day. Therefore, individuals with seasonal problems in mood and behaviour might benefit from this solution.

Photoperiod is the principal responsible of seasonal variations in human organism, especially affecting mental wellbeing. Indoors working subjects exposed to bright light presented improvement in vitality and distress as well as a decrease in their seasonal symptoms (Partonen and Lönnqvist, 2000).

Light synchronizes biological rhythms that are responsible to coordinate actions with the time of the day. On the other hand, monthly and annual cycles regulate the reproductive behaviour. The photoperiod stimulates the retina to reach the suprachiasmatic nuclei located in the hypothalamus. The endocrine (melatonin and cortisol) and the autonomous nervous systems (blood pressure and heart frequency) are influenced by the day-night cycle. Even complex human behaviour such as social contacts and meal times can affect the circadian rhythms (Murguía, 2002).

Physical exercise practiced with bright light exposure show important improvements in seasonal and atypical depressive symptoms such as carbohydrate craving, increased appetite, morning fatigue and increased need for sleep. At the same time, they improve vitality and mood (Partonen et al., 1998a; Partonen and Lönnqvist, 2000; Leppämäki, 2002). In the wintertime these measures seemed to be well tolerated by persons with mild, subsyndromal and severe seasonal symptoms with a higher feeling of self-control and self-confidence (Partonen et al., 1998).

6.7 Strengths and limitations of the study

A large nationwide sample representative of the Finnish population aged over 30 was included in this study. The results of this study can be generalized to any population that share similar characteristics during that time. Face-to-face interviews, total health examination protocol and a questionnaire delivery composed the method of this study. SPAQ is a retrospective questionnaire that evaluates seasonal variations in a lifetime. It possesses good psychometric properties with an excellent sensitivity and specificity (94% and 73%) for SAD, as well as sub-SAD (Magnusson et al., 1996) and high internal consistency (Magnusson et al., 1997). At the same time it provides the GSS, which is relevant in the evaluation of mood, energy, metabolism and seasonal mental health in the general population (Murray et al., 2003). Indoors illumination self-reports provided relevant hazardous indicators of lighting conditions at home and at work.

The validity and reliability of the M-CIDI interview has been tested in large surveys (Wittchen et al., 1998; Kessler et al., 2003). The definition of metabolic syndrome given by the NCEP-ATPIII is based on risk factors grouped in categories that can be applied in the general population. Patients with type 2 diabetes as well as individuals with metabolic syndrome is associated with an increased cardiovascular morbidity and mortality (Isomaa et al., 2001; Resnick et al., 2003).

The evaluation of the repeatability and stability of the 15D was rated as good (Sintonen, 1995). Concerning its test-retest reliability it was evidently better than other instruments (Stavem, 1999). An extensive survey was undertaken so as to test the validity of the 15D at a population level. The results showed that the 15D scores were valid and the best for Quality of life adjusted year calculations (www.15d-instrument.net).

The design used to measure seasonal variations in mood and behaviour was cross-sectional, which does not allow conclusive causal explanations. In addition, the measurements of seasonal variations and indoors illumination were based on self-reports as part of an interview. Due to the fact that illumination was evaluated with only two items, it cannot be taken as a precise measurement for light exposure. SPAQ is not recommended either to detect diagnostic cases for mental disorders (Thompson et al., 2004) nor compare seasonal variations in populations living in different geographic settings (Lund and Hansen, 2001).

6.8 Implications for clinical work

SAD and depression present problems in the circadian rhythm that can be corrected by natural/artificial light as well as physical exercise for fitness purposes. Partonen et al. (1998) found improvement in quality of life and mental well-being as well. Photoperiod seems an important factor that influences changes in the biological clock, metabolism, mood and behaviour. Therefore, all individuals should take advantage of light, specifically in the mornings and if they practice a physical routine.

There are cases in which persons with seasonal and depressive symptoms complain from a poor illumination at home and at work, which decreases their daily function in general. Therefore, it would be necessary to re-evaluate the need to improve the illumination conditions, especially indoors in houses and offices that could be designed better than they are currently. They have to take into account how light affects circadian and metabolic rhythms and regulate the level of energy to experience mood and behaviour. One issue that concerns architects is that houses and offices should not reflect seasonal and temporal variations. So, architectural solutions are not just to improve the subjective perception of light, but it should be reflected in the general well-being.

Circadian and metabolic disorders are important health risks that affect the quality of life and mental well-being. Improved architectural designs and self-care in seasonal changes in mood and behaviour could be practical solutions to manage seasonal symptoms. The importance to study the circadian clocks in relation to any source of light (light box, dawn simulation, etc.) is crucial either in clinical or epidemiological settings. Implications in medicine are diverse, especially in diseases such as hypertension, type II diabetes, breast and prostate cancer, depressive disorder, manic-depressive disorder, etc. When physiology is viewed by its temporal dynamics, cycles of gene expression and the role of the hormones in synchronizing such functions, we can have a broad view of the relationship between circadian clocks, health and disease. Daily cycles are in harmony with solar and social rhythms (Hastings et al., 2007).

6.9 Suggestions for future research

There are many factors that influence circadian disruptions in metabolic health, by increasing the risks of metabolic syndrome, hypertension and gastrointestinal disorders in shift workers (Knutsson, 2003; Oishi et al., 2006; Sookoian et al., 2007 for review see Hastings et al., 2007). The genetic and molecular origins of the circadian rhythms provide a better perspective of the effects of circadian disorders on the genes that regulate the cardiovascular system, the control of lipids and carbohydrate metabolism. Cancer would be the most severe pathological expression of the circadian disruptions. Rotating shift workers have a higher risk of developing not just cancers, but growth factor expression or the endocrine environment by changing their clock immune-competence. Oral mucosa and skin proliferating tissues are strongly influenced by the circadian cycle of cell division (Bjarnason et al. 2001; Schernhammer et al. 2003; Hastings et al., 2007).

The deep study of molecular and cellular bases of biological clocks has become a priority for a better knowledge in physiology, by showing how temporal disorganization can originate pathology. At the same time it brings opportunities to develop therapies utilizing central and local clockworks to manage and exploit circadian pathological processes (Hastings et al., 2007). Seasonality as a dimensional factor conceives changes in mood and behaviour as part of a physiological and mental reaction towards the environment. On the other hand, SAD follows different pathophysiological mechanisms, such as delayed phase-shifted circadian rhythms, serotonergic disfunction and genetic vulnerability which has to be further explained (Lam and Levitan, 2000).

6.10 Architectural light as a viable solution to seasonal variation

Living beings are very sensitive to changes of light, even though they come from artificial sources. Its intensity, spatial and temporal dispersion can have a significant influence, depending on the time of the day; it is more efficient in the mornings and in the evenings. Phototherapy has beneficial effects on health and it has been used to recover the synchronization of biological rhythm (Lewy et al., 1988). According to Czeisler's et al. (1990) studies, the white bright light produces fast and intensive changes in the circadian rhythm like a "passive preventive phototherapy". Therefore, the illumination designers began to improve the indoors illumination conditions, taking into account level of illumination, direction, temperature and chromatic reproduction.

Any kind of light either from natural or artificial source has some influence on the biological clock. In order to reach therapeutic effects the light needs to be bright and white. Indoors environment requires as well a light ceiling, walls and floors. Levels of indoors illumination are too low to activate the biological clock and some technical solutions should be implemented to stimulate the SCN via visual path (Küller, 2002). Individuals during shift work usually tend to maintain a diurnal rhythm, which may cause tiredness and a possible risk of accidents. Therefore, bright light during the night should be used as a solution to these negative effects (Küller, 2002).

An adequate illumination design contains the quality of illumination that depends on spatial orientation, phototropic content, contrast, color performance, temperature and blinking (Murguía, 2002). Other recommendations provided by the International Committee of Illumination are visibility, visual satisfaction, execution potential, attitude toward task performance, visual performance, critical detail, level of adaptation, factor and direction of illumination. This committee also recommended the scales of lux used that vary from 20 to 5000, according to the visual demand required by diverse tasks. Mornings and evenings are adequate periods to apply light therapy so as to treat circadian disruption symptoms, such as insomnia or early awakening. It has been successful too, in the alleviation of fatigue and depression during autumn and winter. When time is spent indoors, an adequate provision of light though windows especially during the winter is essential; otherwise, it might have a negative effect on personal well-being and work capacity, for instance underground (Küller, 2002).

Long periods inside windowless or dark environments may increase SAD and sub-SAD symptoms, such as fatigue and lack of energy. The static conditions of artificial light would make more difficult the coordination between the biological and the solar clock in the autumn, winter and spring. Practical solutions to these symptoms would be to work closer to a window and in a proper illuminated room (Küller et al., 1999).

The duration and time of exposure to light has to be enough to make work the circadian clock so as not to suffer from depression or stress. Lifestyle is also a factor which influences biological rhythms. Eating moderately and exercising regularly can stimulate the master circadian clock (Molin et al., 1996). On the other hand, electrical and magnetic fields might have some effects on human physiology. Magnetic field is used by some species to orientate and navigate, and the organism is sensitive to geomagnetic changes by chemical photoreceptors not dependant on circadian rhythms (Gegear et al., 2008). Further investigations should be carried out to find more evidence about this phenomenon.

The intensity of depressive symptoms and well-being feeling affects on the experience of seasonal changes as a problem. At the same time, seasonal variations in mood and behaviour provide an estimate of the master circadian function in metabolic and annual cycles. Individuals who live far from the equator present serious disruptions in their circadian rhythms due to the short periods of light in the winter. The most common symptoms are fatigue, sadness and prolonged sleep, which can be treated by organizing physical activities outdoors and increasing indoors illumination which may influence on mood, stress and job performance. The most important factors to take into account in light exposure are intensity, distribution and time; windows receiving natural light would increase mood and mental well-being and one should not rule out the existence of electrical and magnetic fields affecting us.

Long periods in dark environments and without windows may increase seasonal symptoms such as fatigue, lack of energy and depression (Küller et al., 1999). Light therapy would be recommended in cases with insomnia or early awakening as well as fatigue and depression in the autumn or winter. Any kind of light either natural or artificial have some effect on the circadian clock, and bright white light is more effective than coloured light. It is important to consider the fact that the level of indoors illumination is lower than the standard recommended during the winter mornings.

7 Conclusions

This study released results that allowed answering the questions asked previously.

It was found that 85% of the individuals presented seasonal changes, but just 40% reported them as a problem. *Are seasonal and depressive symptoms associated?* Yes, 9% of them scored high both in GSS and BDI.

Can seasonal changes increase the risk of metabolic syndrome? If seasonal symptoms are not regulated by the subjects affected, a risk to develop metabolic syndrome increases considerably. It was discovered by assessing changes in appetite, weight and waist circumference.

SPAQ was a useful tool to measure seasonal variations in mood and behaviour. *Does poor indoor illumination contribute to metabolic syndrome? Can physical exercise and alcohol intake influence seasonal variation? Is waist circumference an indicator of seasonal variations?* The answer is yes in these questions. Mood is reflected by a lack of physical exercise and alcohol intake in moments of irritation and isolation.

Many persons with seasonal symptoms can function well on a daily basis. However, some have reported to have problems with their mood, cognition, physiology and productivity. *Can seasonal symptoms cause a decrease in the quality of life as well as mental well-being? Can poor illumination at home and at work affect mental well-being and quality of life?* If individuals perceive less light, from natural and/or artificial sources at home and at work, their seasonal symptoms increase and report higher scores in GHQ-12, and lower in 15D which means their quality of life and their mental well-being are affected.

8 Acknowledgements

This work was carried out during the years 2005-2008 at the Department of Mental Health and Alcohol Research of the National Public Health Institute and thereafter in 2009 at the Department of Mental Health and Substance Abuse Services of the National Institute for Health and Welfare. I wish to thank the General Director, Professor Pekka Puska for the facilities provided to me by the two institutes. I want to thank Professor Jouko Lönnqvist the head of the two departments for all the support he has given me during these years. It is a privilege to work in his department.

I want to thank Professor Jaakko Kaprio the head of the Department of Public Health of the University of Helsinki, for his support and the University of Helsinki as a place to study. I also wish to thank the Doctoral Programs in Public Health for my affiliation, and Yrjö Jahnsson Foundation and Signe and Ane Gyllenberg Foundation for their grants given to me.

The official reviewers of this thesis, Professor Sari Lindeman and Professor Jukka Hintikka are thanked for their constructive and encouraging criticism.

I would describe my life in Finland as Yoko Ono's saying "Season of Glass":

Spring passes and one remembers one's innocence: When I decided to live a new experience in another place I thought about Finland as an option, without any previous knowledge of the country, except of being in the northern part of the world. I would like to thank the persons who considered as a crazy funny idea to continue my student life here, especially my mother with her unconditional support... GRACIAS MAMÁ! To Alma, Monica, Andrea and Sigrid to organize me a goodbye party and wishing me the best in my new adventure... GRACIAS CHICAS!

Summer passes and one remembers one's exuberance: When I arrived for the first time to Finland, I was friendly welcomed by the Tiensuu family who gave me their hand and assisted me in my first cultural shock... KIITOS PALJON. A new summer was offered to me full of green grass and leaves; the loveliest summer since more than 50 years in that time. My impressions were recorded throught my feelings and thoughts until I realized that the summer was gone.

Autumn passes and one remembers one's reverence: I started to realize that each annual phenomenon is reminiscence and prompting, that our thoughts and feelings answer to the revolution of the seasons as transitions in time. Every sensation acquired its own language in nature when I met love and my heart gave a new turn... GRACIAS MI AMOR! A new seed was blooming and turned into a gorgeous baby. Then, a mother was born... GRACIAS MI LEO!

Winter passes and one remembers one's perseverance: If I would have heard Sir Henry Thoreau saying: "Now I am ice, I am sorrel; each experience reduces itself to a mood of the mind" would be the perfect inspiration to find a new opportunity to research. My guides were always there to advise me in every moment... KIITOS MAIKKI ja PEKKA. I confess I never imagined being in THL stage where I met SIRKKA LAAKSO for the first time as a character... KIITOS SIRKKA. Professor Lönnqvist was there as the principal character who got to know my research interests... KIITOS JOPI to open me the door. Thanks to him, Timo appeared in the scene with his patient, friendly and discreet personality to show me the world of light and time in winter blues... KIITOS TIMO. Other key characters enriched the play with their technical and administrative advice... KIITOS TUULA KOSKI, OLLI KIVIRUUSU, TIINA HARA ja JARI HAUKKA. Sharing good company with the girls of the fifth floor and new colleagues has brought to me happy moments during my stay... THANK YOU GUYS.

Helsinki, October 2009

Sharon Grimaldi Toriz

9 References

Abrahamson EE, Moore RY. Lesions of suprachiasmatic nucleus efferents selectively affect rest-activity rhythm. Molecular and Cellular Endocrinology 2006; 252(1-2):46-56.

Arendt T. Biological rhythms: The science of chronobiology. J Roy Coll Phys Lond 1998; 32: 27-35.

Bartness TJ, Demas GE, Song CK. Seasonal changes in adiposity: the roles of the photoperiod, melatonin and other hormones, and sympathetic nervous system. Exp Biol Med 2002;227(6):363-76.

Beck, AT, Steer RA. Internal consistencies of the original and revised Beck Depression Inventory. J Clin Psychol 1984; 40(6):1365-7.

Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch. Gen. Psychiatry 1961; 4: 561-571.

von Bertalanffy, L. An Outline of General Systems Theory. British Journal for the Philosophy of Science 1950; 1(2).

Bhattacharjee Y. Is internal timing key to mental health? Science 2007; 317: 1488-1490.

Bjarnason GA, Jordan RC, Wood PA. Circadian expression of clock genes in human oral mucosa and skin: association with specific cell-cycle phases. Am J Pathol 2001;158(5):1793-801.

Blazer DG, Kessler RC, Swartz MS. Epidemiology of recurrent major and minor depression with a seasonal pattern: the National Comorbidity Survey. Br J Psychiatry 1998; 172: 164-7.

Cai W, Rambaud J, Teboul M, et al. Expression levels of estrogen receptor β are modulated by components of the molecular clock. Molecular and Cellular Biology 2002; 28(2):784-793.

Czeisler C, Johnson M, Duffy J, Brown E, Ronda J, Kronauer R. Exposure to bright light and darkness to treat physiologic maladaptation to night work. New Engl J Med 1990; 322: 1253-1259.

Foster RG and Roenneberg T. Human responses to the geophysical daily, annual and lunar cycles. Current biology 2008; 18(17):784-94.

Gegear RJ, Casselman A, Waddell S, Reppert SM. Cryptochrome mediates light-dependent magnetosensitivity in Drosophila. Nature 2008; 454 (21): 1014-18.

Gillette MU, Sejnowski TJ. Physiology. Biological clocks co-ordinately keep life on time. Science 2005; 309(5738):1196-8.

Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. Psychol Med 1979; 9(1):139-45.

Green CB, Takahashi JS, Bass J. The meter of metabolism. Cell 2008; 134:728-42.

Grimaldi B, Nakahata Y, Kaluzova M, et al. Chromatin remodeling, metabolism and circadian clocks: the interplay of CLOCK and SIRT1. Int J Biochem Cell Biol 2009;41(1):81-6.

Halberg F., Halberg E., Barnum C.P., Bittner J.J.: Physiologic 24-hour periodicity in human beings and mice, the lighting regimen and daily routine. In: Photoperiodism and Related Phenomena in Plants and Animals, Withrow R.B. (ed.), Ed. Publ. #55, Am. Assn. Adv. Sci., Washington, DC, 1959: 803-878.

Hansen V, Lund E, Smith-Siverstern T. Self-reported mental distress under the shifting daylight in the high north. Psychol Med 1998;28: 447-452

Hansen V, Lund E, Smith-Sivertsen T. Self-reported mental distress under the shifting daylight in the high north. Psychol Med 1998; 28: 447-52.

Hays R, Morales L. The RAND-36 measure of health-related quality of life. Ann Med 2001;33:350-357.

Hastings M, O’Neill JS, Maywood ES. Circadian clocks: regulators of endocrine and metabolic rhythms. J Endocrinol. 2007;195(2):187-98.

Heiskanen TH, Niskanen LK, Hintikka JJ et al. Metabolic syndrome and depression: A cross-sectional analysis 2006; 67(9): 1422-27.

Hofstra WA, Weerd AW. How to assess circadian rhythm in humans: A review of the literature. Epilepsy & Behaviour 2008; 13:438-44.

Ilanne-Parikka P, Eriksson JG, Lindström J, et al. Prevalence of the metabolic syndrome and its components. Findings from a Finnish general population sample and the diabetes prevention study. Diabetes Care 2004; 27(9): 2135-40.

Isomaa B, Henricsson M, Almgren P, et al. The metabolic syndrome influences the risk of chronic complications in patients with type II diabetes. Diabetologia. 2001 Sep;44(9):1148-54.

Jane-Llopis E, Hosman C, Jenkins R, Anderson P. Predictors of efficacy in depression prevention programmes: meta-analysis. Br J Psychiatry 2003; 183: 384-97.

Kasper S, Rogers SLB, Yancey A, et al. Phototherapy in Individuals with and without Sub-syndromal Seasonal Affective Disorder. Arch Gen Psychiatry 1989; 46: 837-844.

Kasper S, Wehr TA, Bartko JJ, et al. Epidemiological findings of seasonal changes in mood and behavior. A telephone survey of Montgomery County Maryland. Archives of General Psychiatry 1989; 46(9): 823-833

Kessler RC, Ormel J, Demler O, et al. Comorbid mental disorders account for the role impairment of commonly occurring chronic physical disorders: results from the National Comorbidity Survey. J Occup Environ Med 2003 Dec;45(12):1257-66.

Ko CH, Takahashi JS. Molecular components of the mammalian circadian clock. Hum Mol Genet 2006; 15 Spec No 2:R271-7.

Knutsson A. Health disorders of shift workers. Occup Med (Lond) 2003;53(2):103-8.

Kronholm E, Partonen T, Laatikainen T, et al. Trends in self-reported sleep duration and insomnia-related symptoms in Finland from 1972 to 2005: a comparative review and re-analysis of Finnish population samples. Journal of Sleep Research 2008; 17(1): 54-62.

Kruijver FP, Swaab DF. Sex hormones receptors are present in the human suprachiasmatic nucleus. Neuroendocrinology 2002; 75(5):296-305.

Küller R, Ballal S, Laike T, et al. The impact of light and colour on psychological mood: a cross-cultural study of indoor work environments. Ergonomics 2006; 49(14): 1496-1507.

Küller R, Wetterberg L. The subterranean work environment: Impact on well being and health. En viron Int 1996; 22:33-52.

Küller R, Ballal SG, Laike T, et al. Shortness of daylight as a reason for fatigue and sadness. A cross-cultural comparison. Proceedings CIE 24th session, Warsaw 1999;1(2):291-4.

Küller R. The influence of light on circarhythms in humans. J of Physiological Anthropology 2002; 87-91.

Lam RW, Levitan RD. Pathophysiology of seasonal affective disorder: a review. Journal of Psychiatry & Neuroscience 2000; 25: 469-480.

Leppämäki S, Haukka J, Lönnqvist J, Partonen T. Drop-out and mood improvement: a randomised controlled trial with light exposure and physical exercise. BMC Psychiatry 2004; 4: 22.

Leppämäki S, Meesters Y, Haukka J, Lönnqvist J, Partonen T. Effect of simulated dawn on quality of sleep - a community-based trial. BMC Psychiatry 2003; 3: 14.

Leppämäki S, Partonen T, Hurme, J. Randomized trial of the efficacy of bright-light exposure and aerobic exercise on depressive symptoms and serum lipids. J Clin Psychiatry 2002; 63(4):316-21.

Lewy AJ, Sack RL, Singer CM, et al. Winter depression and the phase-shift hypothesis for bright light’s therapeutic effects: history, theory, and experimental evidence. J Biol Rhythms 1988;3(2):121-34.

Lund E, Hansen V. Responses to the Seasonal Pattern Assessment Questionnaire in different seasons. Am J Psychiatry 2001; 158: 316-8.

Lurie SJ, Gawinski B, Pierce D, et al. Seasonal Affective Disorder Am Fam Physician 2006;74(9):1521-4.

Magnusson A, Axelsson J, Karlsson MM, Oskarsson H. Lack of seasonal mood change in the Icelandic population: results of a cross-sectional study. Am J Psychiatry 2000; 157: 234-8.

Magnusson A, Friis S, Opjordsmoen S. Internal consistency of the Seasonal Pattern Assessment Questionnaire (SPAQ). J. Affect. Disord 1997; 42: 113-116.

Magnusson A. Validation of the Seasonal Pattern Assessment Questionnaire (SPAQ). J. Affect. Disord 1996; 40: 121-129.

Magnusson, A. An overview of epidemiological studies on seasonal affective disorder. Acta Psychiatr Scand 2000; 101: 176-184.

Maquet P. Positron emission tomography studies of sleep and sleep disorders. Neurol 1997; 244(4 Suppl 1):S23-8.

Marchesini G, Forlani F, Cerreli, R et al. WHO and ATPIII proposals for the definition of the metabolic syndrome in patients with Type 2 diabetes. Diabetic Medicine 2004; 21: 383-387.

McCarthy E, Tarrier N, Gregg L. The nature and timing of seasonal affective symptoms and the influence of self-esteem and social support: a longitudinal prospective study. Psychol Med 2002; 32 (8): 1425-34.

McClung CA. Circadian genes, rhythms and the biology of mood disorders. Pharmacology and therapeutics 2007; 114:222-232.

McColl SL, Veitch JA. Full-spectrum fluorescent lighting: a review of its effects on physiology and health. Psychol Med 2001;3:949-64.

McIntyre RS, Soczynska JK, Konarski JZ, et al. Should depressive syndromes be reclassified as metabolic syndrome type II? Annals of Clinical Psychiatry 2007; 19(4): 257-264.

Mersch PP, Middendorp HM, Bouhuys AL, Beersma DG, van den Hoofdakker RH. Seasonal affective disorder and latitude: a review of the literature. J Affect Disord 1999; 53: 35-48. (a)

Mersch, PPA., Middendorp, HM., Bouhuys, AL, Beersma, DGM., van der Hoofdakker, RH. The prevalence of seasonal affective disorder in the Netherlands: A prospective and retrospective study of seasonal mood variation in the general population. Society of Biological Psychiatry 1999; 45: 1013-1022. (b)

Mersch, PPA., Vastenburg, NC., Meesters, Y., Bouhuys, AL., Beersma, DGM., van den Hoofdakker, RH., den Boer JA. The reliability and validity of the seasonal pattern assessment questionnaire: a comparison between patient groups. Journal of affective disorders 2004; 80: 209-219.

Michalak E, Tam E, Manjunath CV et al. Generic and health-related quality of life in patients with seasonal and non seasonal depression. Psychiatry Research 2004; 128:245-251.

Michalak E, Tam E, Manjunath CV, et al. Quality of Life in Patients with Seasonal Affective Disorder: Summer and Winter Scores. Can J Psychiatry 2005; 50(5):292-295.

Michalak EE, Murray G, Levitt A et al. Quality of life as an outcome indicator in patients with seasonal affective disorder: results from the Can-SAD study. Psychol Med 2007; 37(5):1-10.

Michalak EE, Wilkinson C, Hood K, Dowrick C, Wilkinson G. Seasonality, negative life events and social support in a community sample. Br J Psychiatry 2003; 182: 434-8.

Michalak, EE., Wilkinson, C., Dowrick, C., and Wilkinson, G. Seasonal affective disorder: prevalence, detection and current treatment in North Wales. Br J Psychiatry 2001; 179: 31-34.

Molin J, Mellerup E, Bolwig P, et al. The influence of climate on development of winter depression. J Affect Disord 1996; 37: 151-155.

Montazeri A, Mahmood A, Shariati M, et al. The 12-item General health Questionnaire (GHQ-12) translation and validation study of the Iranian version. Health Qual Life Outcomes 2003;1(1):1-66.

Moteleone P, Maj M. The circadian basis of mood disorders: Recent developments and treatment implications. European Neuropsychopharmachology 2008; 18:701-11.

Murguía L. La luz en la Arquitectura. Su influencia sobre la salud de las personas. Estudio sobre la variabilidad del alumbrado artificial en oficinas 2002; Dissertation Universitat Politécnica de Catalunya. http://www.tdx.cat/TDX-0115103-121936.

Murray G. The Seasonal Pattern Assessment Questionnaire as a measure of mood seasonality: a prospective validation study. Psychiatry Res 2003; 120: 53-9.

National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), "Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report," Circulation 2002; 106(25): 3143-421.

Oishi K, Atsumi G, Sugiyama S, et al. Disrupted fat absorption attenuates obesity induced by a high-fat diet in Clock mutant mice. FEBS Lett 2006;580(1):127-30.

van Oort BEH, Tyler NJC, Gerkema MP, et al. Where clocks are redundant: weak circadian mechanisms in reindeer living under polar photic conditions. Naturwissenschaften 2007; 94(3): 183-194.

Orsucci FF. The paradigm of complexity in clinical neurocognitive science.Neuroscientist 2006; 12(5):390-7.

Partonen T, Haukka J, Nevanlinna H, et al. Analysis of the seasonal pattern in suicide. J Affect Disord 2004; 81: 133-39.

Partonen T, Leppämäki S, Hurme J, et al. Randomized trial of physical exercise alone or combined with bright light on mood and health-related quality of life. Psychol Med 1998;28:1359-1364.

Partonen T, Lönnqvist J. Seasonal affective disorder. Lancet 1998; 352: 1369-74.

Partonen T, Lönnqvist, J. Bright light improves vitality and alleviated distress in healthy people. J Affect Disord 2000;55-61.

Partonen T, Partinen M, Lönnqvist J. Frequencies of seasonal major depressive symptoms at high latitudes. Eur Arch Clin Neurosci 1993; 243: 189-192.

Pirkola S, Isometsä E, Suuvisaari J, et al. DSM-IV mood, anxiety- and alcohol use disorders and their comorbity in the Finnish general population; Results from the Health 2000. Soc Psychiatry Psychiatr Epidemiol 2005; 40: 1-10.

Polgar M. Beck Depression Inventory. Gale encyclopedia for mental disorders 2003. http://www.encyclopedia.com/doc/1G2-3405700046.html

Preti A. The influence of seasonal change of suicidal behaviour in Italy. J Affect Disord 1997; 44(2-3): 123-30.

Resnick HE, Jones K, Ruotolo G, et al. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease in nondiabetic American indians: the Strong Heart Study. Diabetes Care. 2003;26(3):861-7.

Rivest RW, Schultz P, Lustenberger S, Sizonenko PC. Differences between circadian and ultradian organization of cortisol and melatonin rhythms during activity and rest. J Clin Endocr Metab 1989; 68:721-729.

Roenneberg T, Aschoff J. Annual rhythm of human reproduction: I. Biology, sociology or both? J Biol Rhythms 1990; 5(3): 195-216.

Rosenthal NE, Bradt GH, Wehr TA. Seasonal Pattern Assessment Questionnaire. National Institute of Mental Health: Bethesda, 1984. (a)

Rosenthal NE, Sack D A, Gillin JC, et al. Seasonal affective disorder: description of the syndrome and preliminary findings with light therapy. Archives of General Psychiatry 1984;41:72-80. (b)

Rotter, JB. Social learning and clinical psychology. New York 1954: Prentice-Hall.

Saarijärvi S, Lauerma H, Helenius H, Saarilehto S. Seasonal affective disorders among rural Finns and Lapps. Acta Psychiatr Scand 1999; 99: 95-101.

Sakurai T. The neural circuit of orexin (hypocretin): maintaining sleep and wakefulness Nature Reviews Neuroscience 2007; 8,(3): 171-181.

Scheer FA, Wright KP Jr, Kronauer RE, et al. Plasticity of the intrinsic period of the human circadian timing system. PLoS One 2007; 2(1):e721.

Schernhammer ES, Laden F, Speizer FE, et al. Night-shift work and risk of colorectal cancer in the nurses' health study. J Natl Cancer Inst. 2003 Jun 4; 95(11):825-8.

Sintonen H. The 15D-measure of health-related quality of life. II. Feasibility, reliability and validity of its valuation system. National Centre for Health Program Evaluation, Working Paper 42, Melbourne 1995.

Sintonen H. The 15D instrument of health-related quality of life properties and applications. Ann Med 2001;33: 328-336.

Sohn CH, Lam RW. Update on the biology of seasonal affective disorder CNS Spectr 2005; 10(8): 635-46.

Sookoian S, Gemma C, Gianotti TF, et al. Serotonin and serotonin transporter gene variant in rotating shift workers. Sleep. 2007 Aug 1; 30(8):1049-53.

Stavem K. Reliability, validity and responsiveness of two multi-attribute utility measures in patients with chronic obstructive pulmonary disease. Qual Life Res 1999; 8: 45-54.

Storch KF, Paz C, Signorovitch J, et al. Physiological importance of a circadian clock outside the suprachiasmatic nucleus. Cold Spring Harb Symp Quant Biol 2007;72:307-18.

Takahashi JS, Hong HK, Ko CH et al. The genetics of mammalian circadian order and disorder: implications for physiology and disease. Nature 2008; 9:764-75.

Teicher MH, Glod CA, Magnus E, et al. Circadian rest-activity disturbances in seasonal affective disorder. Arch Gen Psychiatry 1997;54(2):124-30.

Terman M, White TM, Fairhurst S, et al. Predictors of winter depression: Latitude and longitude in relation to photoperiod and sunrise. Soc Light Treat Biol Rhythms Abstr 2008; 20:56-7.

Tiihonen J, Räsänen P, Hakko H. Seasonal variation in the occurrence of homicide in Finland Am J Psychiatry 1997; 154(12):1711-4.

Thompson C, Childs PA, Martin NJ, et al. Effects of morning phototherapy on circadian markers in seasonal affective disorder. Br J Psychiatry. 1997;170:431-435.

Thompson C, Thompson S, Smith R. Prevalence of seasonal affective disorder in primary care; a comparison of the seasonal health questionnaire and the seasonal pattern assessment questionnaire. J Affect Disord 2004; 78: 219-26.

Thorpy MJ, Yager J, eds. The encyclopedia of sleep and sleep disorders. New York: Facts on File, 1991: 85.

Tonello, G. Lighting, Mood, and Seasonal Fatigue in Northern Argentina. Comparison to Countries Close to and Further from the Equator, 2001; Dissertation Lund University.

Tu BP, McKnight SL. Metabolic cycles as an underlying basis of biological oscillations. Nat Rev Mol Cell Biol. 2006;7:696-701.

Tuomilehto J. Cardiovascular risk: prevention and treatment of the metabolic syndrome. Diabetes Res Clin Pract. 2005; 68 2:S28-35.

Vondrasova JD, Hajek I, Illnerova H. Adjustment of the human melatonin and cortisol rhythms to shortening of the natural summer photoperiod. 1999; 816: 249-25

Wicki W, Angst J, Merikangas KR. The Zurich study. XVI. Epidemiology of seasonal depression. Eur Arch Psychiatry Clin Neurosci 1992; 241(5):301-6.

Wittchen HU, Lachner G, Wunderlich U, et al. Test-retest reliability of the computerized DSM-IV version of the Munich-Composite International Diagnostic Interview (M-CIDI). Soc Psychiatry Psychiatr Epidemiol. 1998; 33(11):568-78.

World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. Geneva, Switzerland: World Health Organization, 2000. (WHO technical report series, 894).

Yanovski JA, Yanovski SZ, Sovik KN, et al. A prospective study of holiday weight gain. N Engl J Med. 2000; 342(12):861-7.

Yerushalmi S and Green RM. Evidence for the adaptative significance of circadian rhythms. Ecology Letters 2009; 12: 970-81.

Young MA. Integrating psychological and physiological mechanisms of SAD: the dual-vulnerability model. Biological Rhythms Bulletin 1999; 1: 4-6.

Young MA, Meaden PM, Fogg LF, et al. Which environmental variables are related to the onset of seasonal affective disorder? Abnorm Psychol. 1997; 106(4):554-62.

Young MA, Watel LG, Lahmeyer HW, et al. The temporal onset of individual symptoms in winter depression: differentiating underlying mechanisms. J Affect Disord 1991; 22: 191-197.

Zambon AC, McDearmon EL, Salomonis N, et al. Time- and exercise-dependent gene regulation in human skeletal muscle. Genome Biology 2003; 4(10):1-12.

Zhang J, Kaasik K, Blackburn MR, Lee CC. Constant darkness is a circadian metabolic signal in mammals. Nature. 2006; 439:340-343.