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CIRCADIAN RHYTHM FACTOR IN THE ANALYSIS AND INTERPRETATION OF INFRARED THERMOGRAPHY RESULTS IN THE ARCTIC (Review) = = РОЛЬ ЦИРКАДНЫХ РИТМОВ В АНАЛИЗЕ И ИНТЕРПРЕТАЦИИ РЕЗУЛЬТАТОВ ИНФРАКРАСНОЙ ТЕРМОГРАФИИ В АРКТИКЕ (обзор)[1]

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Научные работы, в которых объясняется влияние факторов окружающей среды Арктики на проведение исследований с использованием метода инфракрасной термографии, на данный момент немногочисленны. Цель данной статьи – рассмотреть циркадные ритмы, которые могут влиять как на выполнение анализа, так и на интерпретацию результатов инфракрасной термографии в Арктике. Изучены научные работы, опубликованные в период с 1981 по 2019 год. Статьи были идентифицированы с помощью поисковых систем PubMed посредством систематического онлайн-поиска в базе данных по ключевым словам «инфракрасная термография» и с использованием системы PRISMA. После изучения аннотаций к подходящим статьям с полным доступом было отобрано более 80 работ, из них 15 российских, 11 канадских, 3 финских, 40 американских, 2 норвежские, 6 шведских и 4 датских. После проверки материалов и методов в данных статьях на предмет соответствия области применения (медицина и стоматология) 12 статей были признаны полностью отвечающими критериям отбора для данного исследования. Их анализ показал, что, учитывая влияние различной освещенности и продолжительности дня в Арктике, можно отметить три регулятора циркадного ритма, обусловливающих физиологическое изменение его активности: свет достаточной интенсивности, супрахиазматические ядра и нейромедиаторы. Их влияние часто снижается летом и связано с

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изменением температуры кожи. Исследователям необходимо учитывать время дня, сезон и режим сна обследуемого для определения необходимости его включения или исключения из выборки, чтобы провести точное измерение температуры методом инфракрасной термографии.

Ключевые слова: *Арктика, циркадные ритмы, инфракрасная термография, интенсивность света, мелатонин, нейромедиатор, супрахиазматические ядра.*

Presently, thermal pattern of the body is one of the best indicators of health status in humans. Thermal configuration of the body can indicate changes taking place in it, thus being a potential sign of a pathological process [1]. Heat pattern examination is believed to enhance the success of the most common treatment protocols. Any pathological condition, locally or generally, affects the processes of heat production and heat transfer in the body [1]. One of the modern methods of recording temperature of the examined area is infrared thermography. It detects the natural thermal radiation of the human body in the invisible infrared region of the electromagnetic spectrum [2].

Since infrared thermography is known for its ability to detect many groups of diseases at once, its use as a diagnostic tool in humans has been expanding. This approach enables both medical and veterinary practitioners to specify the localization of supposed changes and discover signs of a disease at a symptom-free stage. The informational content and reliability of thermal imaging are close to 100 % and for primary examinations, to 80 % [3]. Moreover, this non-invasive and low-cost technique causes no discomfort in patients, is easy to execute and totally harmless even with frequent use. Importantly, infrared thermography can be safely applied in pregnant women and young children as it produces no effect on their health [4].

One of the method's disadvantages, however, is that it can be influenced by external factors. In particular, the circadian rhythm can be affected by the natural characteristics of the environment in which the thermographic examination is conducted. Unlike individual factors, circadian rhythms are very difficult to control in the Arctic.

To date, there are few studies dealing with the effect produced by circadian rhythms of indigenous and non-indigenous residents of the Arctic on the results of infrared thermography. This paper looks at the circadian rhythm as a factor influencing both the analysis and interpretation of infrared thermograms in the Arctic.

Living in the Arctic entails the ability to adapt to extreme cold, day length and, in some cases, isolation for long periods of time. Geographically, the Arctic includes Canada, Greenland, Denmark, Iceland, Norway, Sweden, Finland, Alaska and northern areas of Russia with the Arctic climate [5]. The population of the Arctic regions is around four million people, spread over a large geographical area in an ecosystem highly adapted to a harsh and sensitive climate. Many indigenous residents live and work with limited access to daylight and in low temperatures. Meanwhile, the environmental factor of the Arctic poses diverse health risks not only for the indigenous residents. According to the United States Centers for Disease Control and Prevention (CDC), 63 % of weather-related deaths between 2006 and 2010 in the United States were attributed to cold exposure, while only 31 % were attributed to heat exposure [6]. The temperature in the Arctic recorded at the latitude 75° south of the Equator can fall below −50 °C. Obviously, protective clothing and mostly indoor work in the winter will reduce exposure to extreme cold [7].

One of the reasons behind the growing number of temporary residents in the Arctic is foreign students, who mostly come from tropical countries. In 2016, Russian universities enrolled 244,597 foreign students. Over the year that followed, the number of students from tropical countries in Russian universities increased by

17 %, the number of students from India increased by 20 %, and those from China, by 10 %. The Russian Ministry of Education reports that in 2015–2016 Russian universities enrolled about 3.1 thousand people from Vietnam and about 11 thousand from African countries [6].

The principle of infrared thermography is to detect and calculate differences in the heat emitted by the body within the variety of background infrared emission and convert them into electrical signals [7]. Infrared thermography cameras convert infrared radiation into an electric output. The camera receives emission from the target object as well as emission from its surroundings that has been reflected onto the object's surface. Both of these radiation components become attenuated while passing through the atmosphere. Consequently, an overriding issue is matching the detector's response curve to the atmospheric window [8, 9].

As is well known, infrared thermography procedure is based on physics equations [10]. For a body, the energy emitted in the infrared region per unit surface area per unit time (emissive power) is determined by the total radiation power and depends on the body's temperature. This is demonstrated in Equation 1 below [11]:

$$E = \varepsilon\, \sigma\, T^4, \quad (1)$$

where σ (the Stefan–Boltzmann constant) is $5.67{\cdot}10^{-8}$ $W{\cdot}m^{-2}{\cdot}K^{-4}$, and ε is body emissivity. In the case of a perfect blackbody, ε = 1. For human skin, ε = 0.98.

Cameras capture both the heat radiated by the body and that reflected by it (*Eq*. 2). It is crucial to determine the reflected temperature of the camera to obtain the surface temperature of the body (*T*) (*Eq*. 3):

$$E_{received} = \varepsilon\, \sigma\, T^4 + (1 - \varepsilon)\, \sigma\, T^4_{reflected}; \quad (2)$$

$$t = \{[\, E_{received} - (1 - \varepsilon)\, \sigma\, T_{reflected}] \,/\, \varepsilon\, \sigma\}^{1/4}, \quad (3)$$

where *T* is the surface temperature and σ equals $5.67{\cdot}10^{-8}$ $W{\cdot}m^{-2}{\cdot}K^{-4}$.

Based on the two physics ideas above, temperature fluctuations can alter the emissive power, which can influence both the analysis and interpretation of thermograms.

Furthermore, cold temperatures, adverse weather conditions, and prevailing darkness in the winter are among the many challenges of making research in the Arctic. People living in these areas can experience more sleep problems and seasonal variations in sleep patterns than those living in tropical countries. In many cases, during the winter, non-indigenous residents are limited in mobility, which causes desynchronization of sleep. This indicates that changes in the circadian rhythms of both indigenous and non-indigenous residents of the Arctic may affect the interpretation of the obtained thermograms. Temperature-related variations in sleep patterns have the potential of producing biased results and increase the risk of unfavourable outcome. These conditions may influence the biological process known as the circadian rhythm. It is generally acknowledged that the daily light–dark cycle determines the rhythmic changes in people's behaviour and/or physiology. Studies have found that these changes are governed by the biological clock, which in humans is located in two brain areas called the suprachiasmatic nuclei. Moreover, the circadian cycle can be synchronized depending on light intensity and secretion of melatonin [8]. Thus, there are four reasons why circadian rhythm matters in infrared thermography in the Arctic. They are as follows: light intensity, suprachiasmatic nucleus, neurotransmitter, and melatonin.

1. Light intensity. Changes in circadian rhythm in the Arctic could be related to light of sufficient intensity, which is the main factor that maintains the 24-hour period of human circadian rhythms. In the Arctic, people lack natural sunlight in the winter and are exposed to continuous daylight in the summer. The typical impact during the winter months is increased insomnia; sleep problems have been reported more often during the winter than during the summer. The sun in the Arctic is absent from mid-November to mid-January. However, it is never pitch black even during the winter solstice. At midday, the sky is still of a deep blue colour, but the intensity is dim and day length is short [12]. Consequently, permanent exposure

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to these conditions can cause sleep problems for people living in the Arctic.

Moreover, the circadian rhythm and its influence on body temperature demonstrated that skin temperature is higher in the evening and more stable until noon. It is confirmed that daily activity directly affects skin temperature variations. Humans are more active in places with sufficient lighting. This has been proven by interesting findings that describe the effect of circadian rhythms depending on the area of light intensity [13].

A comprehensive analysis of external and internal factors of a wide range of studies related to cold areas needs to be undertaken. Although research results include a comprehensive strategy for applying infrared thermography in cold areas, the evidence needs to be generalized for a more accurate identification of the light intensity factor in selecting inclusion and exclusion criteria for non-indigenous research participants. The standard of the American Academy of Thermology is often used to map the criteria in a cold area context to obtain a more reliable result [14]. Hence, such studies should provide methods which support empirical research. Otherwise, they can prove difficult to replicate and can be biased as the review they are based on may not be comprehensive.

The physiology of indigenous and non-indigenous residents of the Arctic is of interest and concern. Evidence indicates that during the Arctic winter, the circadian rhythm is disrupted due to the lack of bright sunlight. Physiological alteration caused by the long winter evenings can be successfully treated with additional bright light that mimics a long summer day. For various reasons, people, especially non-indigenous residents, move to higher latitudes than their previous areas of residence. It is well known that the higher the latitude, the more days with no sunlight or continuous sunlight. In the winter and summer, the sun has different phases. The greatest light exposure attainable during the winter, with an orange glow on the horizon at noon and some areas using artificial light, is 500–700 lux, whereas on a bright sunny day in July, outdoor light intensity in colder regions can reach 40,000 lux, while in temperate/equatorial zones it can reach 100,000 lux [15].

Furthermore, in indoor workspaces, illumination rarely exceeds 300–500 lux; whereas when the sun is below the horizon (as at night or during the prolonged Arctic winter), outdoor illumination is seldom greater than 100 lux and is generally less than 1 lux. This demonstrates that the light–dark cycle in the Arctic is reliant on artificial light in the winter. Artificial light differs from natural light in terms of both quantity and quality (e.g. brightness, spectral composition). It also lacks fluctuation due to geographical distribution, seasonal change, and the 24-hour light–dark cycle. All of these factors have an impact not only on one's efficiency, but also on communication between people [16].

Many earlier studies on humans have found a strong relationship between sleep and thermoregulation, which is largely governed by circadian rhythms and sleep regulation. Humans have a sleep–wake cycle that repeats itself every 24 hours. In a 24-hour circadian rhythm, the core body temperature (T_{core}), which also cycles with the sleep–wake rhythm, goes down during the nocturnal sleep and increases at awakening [17].

When T_{core} falls due to the lack of natural daylight in the winter and also under some conditions in the summer, sleep is more likely to occur. T_{core} goes down in humans during the usual sleep onset phase due to an underlying circadian cycle, with sleep amplifying this impact [18]. Consequently, peripheral skin temperature, rich in arteriovenous anastomoses, plays a crucial role in thermoregulation. Increased peripheral skin temperature is mostly due to decreased noradrenergic vasoconstrictor tone, which allows more hot blood from the core to flow to the skin surface. The drop in T_{core} at sleep onset is also linked to cardiac autonomic activity. Variations in the cardiac autonomic nervous system may precede the onset of sleep, which is strongly linked to changes in body temperature.

2. Suprachiasmatic nucleus. The suprachiasmatic nucleus (SCN), acting as a circadian pacemaker, has the function of orchestrating the timing in physiology and behaviour. While determining the circadian rhythm, the SCN is affected by the natural light–dark cycle. Moreover, the SCN is known to perform photoreceptive and phototransductive functions [19].

It has been established that the SCN responds to the light entering the eye and thus is sensitive to the cycles of day and night. In the evening, T_{core} and proximal skin temperature rise in contrast to distal skin temperature, while the opposite effect seems to take place in the morning [20]. During this time, the light relayed from the retina reaches the SCN in the hypothalamus and the production of neurotransmitters in the pineal gland is suppressed. In the evening, neurotransmitter secretion again increases, thus inducing drowsiness. Light, in this case, acts as a trigger, and the SCN transforms this information into neural signals that set the body's temperature. This is owing to the sympathetic nervous system's effect and the body's tendency to lower skin temperature.

Inflammatory lesions, on the other hand, are easily localized in cool temperatures, resulting in thermal imbalance between the left and the right sides of the body. Infrared thermography is recognized as having a critical role in the assessment of inflammation [21]. As stated in previous studies, the rate of organic chemistry processes decreases in inflammation, while the intensity of separated processes of cellular respiration and phosphorylation can increase. As a result, the temperature of the inflamed area will be higher than that of the surrounding tissue [22]. Consequently, a small change in internal body temperature automatically affects the intensity of cell functions, while changes in the heat emitted by the body (electromagnetic radiation) are detected by the thermal imager, resulting in thermograms. This can influence the interpretation of thermal images.

3. Neurotransmitters. Studies have indicated the presence of a large number of neurotransmitters in the SCN. The existence of neurotransmitters in the SCN's afferent and efferent projections is shown to be equally crucial for the clock's entrainment and control of overt rhythms. According to one study, the specific roles of various neurotransmitters may be based on the response of SCN neurons to neurotransmitter application, capacity to phase shift a particular rhythm in response to neurotransmitter application, effect of lesions on entrained and free-running rhythms, and disruptions seen in the rhythms after blockade by an antagonist/inhibitors. The clock genes *per1* and *per2*, which are activated in the SCN by the light or neurotransmitters at night, have been identified as prospective targets for several neurotransmitters. The SCN's function has been linked to such neurotransmitters as acetylcholine (ACh), glutamate, neuropeptide Y (NPY), serotonin, vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), and arginine vasopressin (AVP) [23].

ACh holds the distinction of being the first neurotransmitter to be recognized as being involved in the regulation of circadian rhythms. It plays a role in the light-input pathway in the SCN, and muscarinic receptors of the M1 subtype are responsible for the action. However, ACh does not appear to be directly involved as a neurotransmitter in the light-input pathway. It may influence the way that photic information reaches the SCN. The main neurotransmitter of the retinohypothalamic tract (RHT) is glutamate. The RHT secretes glutamate directly into the ventral region of the SCN in response to light stimulation of the retina [23].

Photoperiodic and non-photic entrainment of circadian rhythms related to the intergeniculate leaflet (IGL) is mediated by the NPY response to light [24]. Via a separate branch of the RHT, the IGL receives input directly from the retina. The projection from the IGL via the geniculohypothalamic tract (GHT) ends in the areas of the SCN that overlap the direct RHT-SCN input. More evidence exists to support the importance of the GHT in causing non-photic phase shifts during the day but not at night, such as the phase shifts evoked by activity induced by novel stimuli [23].

Serotonin (5HT) is projected from midbrain raphe nuclei to the SCN. Numerous studies suggest

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that the serotonergic projection from the raphe to the SCN is the physical underpinning for affective disorders that disrupt the human circadian system. The modulation of pacemaker responses to light is most likely the main function of the serotonergic projection. Raphe nuclei receive retinal afferents, so the raphe-retina projection can be thought of as an additional indirect photic input to the biological clock [23].

VIPs are activated by the light, and exogenous application of VIP can reset the circadian clock *in vitro* and *in vivo* in a similar way to light application. In the SCN, VIP can help with both mild resetting and maintaining continuous rhythmicity [25]. Previous research revealed that changes in peptide content caused by light conditions could reflect changes in peptide synthesis and release. The release of these peptides varies according to the time of day.

AVP has a major excitatory effect on the SCN, increasing the amplitude of firing rates and improving SCN output during subjective day. It has been suggested that AVP plays a role in the SCN not only in circadian timing but also in the circadian memory of radical events. Decreased amplitude of activity rhythms, increased rhythm fragmentation, and disturbance of the normal sleep–wake cycle have all been linked to a decrease in AVP neurons and AVP levels in the SCN. Many rhythms have been observed to be eliminated or reduced in amplitude when AVP neurons in the SCN are reduced [26].

4. Melatonin. Melatonin, known as an important factor for sleep–wake cycles, is influenced by the light and affects the circadian rhythms and sleep timing. In the SCN, melatonin has a dual effect, direct effects and long-term effects. As a direct effect, melatonin is found to suppress neuronal SCN activity at night [27].

Light inhibits melatonin synthesis in addition to adjusting the SCN. Plasma melatonin levels are low during the day and high at night because melatonin is rapidly absorbed. The dim light melatonin onset, or the initial surge in melatonin release in the early hours of the night when light levels are low, is a consistent and accurate indicator of the intrinsic circadian phase [28].

In the course of one study, melatonin profiles were normal in the summer (high night-time and low daytime levels), whereas in the winter, significantly more – eight profiles – were abnormal (additional daytime peak, out-of-phase daytime secretion, or absence of secretion), of which three (plus one for other reasons) could not be included in further analysis [29]. Another study in the same paper has stated that, as the length of the night changes with seasons, the duration of melatonin secretion increases, resulting in its higher production in the winter than in the summer.

Skin temperature facilitates a rapid start of sleep, and it is highly linked with melatonin secretion. As mentioned in regard to light and the SCN producing sleep disorders which can reduce T_{core}, this condition may change the blood flow to the skin in order to maintain thermoregulation [30]. The change in the blood flow affects skin temperature, and when researchers obtain data through infrared thermography, this approach allows them to analyse and interpret skin temperature as actual temperature of the body.

Due to the effects of different day lengths and different light intensities in the Arctic, the activity of three physiological regulators of the human circadian system – suprachiasmatic nuclei, neurotransmitters and melatonin – changes. These factors are frequently delayed in the summer and physiologically linked with changes in skin temperature. A small change in skin temperature can significantly influence the interpretation of thermal images. Thus, it is important for researchers to consider time, season, and sleep regulation to determine both inclusion and exclusion of participants in order to obtain skin temperature through infrared thermography applications.

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CIRCADIAN RHYTHM FACTOR IN THE ANALYSIS AND INTERPRETATION OF INFRARED THERMOGRAPHY RESULTS IN THE ARCTIC (Review)

The number of studies explaining the role of environmental factors in research using infrared thermography in the Arctic is still limited. This article is focused on circadian rhythms, which can influence both the analysis and interpretation of infrared thermography results in the Arctic. Literature published between 1981 and 2019 was selected with the help of PubMed search engine by means of a systematic search by the keyword *infrared thermography* using the PRISMA system. Having studied the abstracts of relevant open access articles, we selected a total of 81 papers: 40 American, 15 Russian, 11 Canadian, 6 Swedish, 4 Danish, 3 Finnish, and 2 Norwegian. Having assessed the materials and methods against the area of application (medicine and dentistry), we found 12 articles in full compliance with the selection criteria. In conclusion, taking into account different day lengths and light intensities in the Arctic, we point out three circadian rhythm mediators affecting its physiological activity. These are as follows: light of sufficient intensity, suprachiasmatic nuclei and neurotransmitters. Their influence is often reduced in the summer and is linked with changes in skin temperature. Therefore, it is important for researchers to consider time, season, and sleep patterns of the subjects during the selection process in order to obtain accurate temperature measurements using infrared thermography.

Keywords: *Arctic, circadian rhythms, infrared thermography, light intensity, melatonin, neurotransmitter, suprachiasmatic nuclei.*

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