ACHIEVING A MAXIMUM PROGRAM FOR CREATING AND MAINTAINING THE HUMAN WORKFORCE BY OPTIMIZING THE CIRCADIAN SLEEP-WAKE AND FASTING-EATING CYCLES

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REALIZAREA UNUI PROGRAM MAXIM PENTRU CREAREA ȘI MENTINEREA FORȚEI DE MUNCĂ UMANE PRIN OPTIMIZAREA CICLURILOR CIRCADIENE DE SOMN-VEGHE ȘI CELOR POST CONSUM DE ALIMENTE

O analiză sintetică și o modelare experimentală pe animale a activității fizice forțate de desincronizare, combinată cu nutriția hedonică în timpul perioadelor de activitate și odihnă, e necesară pentru a identifica efectul muncii în turele de noapte. Se presupune că desincronizarea forțată și expunerea emoțională comportamentală alimentară produc activarea ***s****inergetică a oscilatorilor centrali hipotalamici laterali suprachiasmatici și orexinergici. Activarea oscilatorilor în timpul perioadei de repaus (orele de zi) distruge ritmul circadian natural și reacțiile bioritmice metabolice naturale.*

Introduction

This work was carried out within the framework of 2 projects: „Neuroprotection and Neurorehabilitation Program based on the combined multimodal action of environmental factors, individual daily activity and ecological nutrition" (postdoctoral project, 22.00208.7007.08/PD I) and "The role of the orexinergic system of the brain in the regulation of the wake-sleep cycle and eating behavior" (doctoral project), funded by the National Agency for Research and Development. The subject of the Projects is devoted to the most pressing problem of modern society, actively involved in daily educational and professional activities, - Optimizing, Respecting the daily regimen of food, work and rest. The implementation of the projects is inspired by the Global Strategy for the Development, Creation and Strengthening of Human Resources: Workforce 2030. Participating countries at all levels of socio-economic development face, to varying degrees, challenges in the fields of Education, Development, Retention and Force Performance of work, i.e. Human Resources. Countries in military conflicts, natural or man-made disasters, those that host refugees and those with vulnerability to climate change, encounter particular difficulties in the creation and development of the Society's Workforce. The links to economic performance in communities and nations are becoming increasingly apparent. This adds to the rationale for strong Global and National policies for Climate Change Mitigation and Adaptation. There is a clear relationship between workplace conditions and Economic Performance and Sustainable Development. If the percentage loss of annual "Productive Work Hours" reduces annual GDP for countries similarly, the losses will be substantial. I am referring to Tord Kjellstrom's article which is related to Climate Change, Human Security, Health, Risk and Vulnerabilities, Economic Development [1]. The Norwegian K. Rodahl, in his work systematizes the factors affecting Physical Performance determined by Training and Adaptation [2].

The International Labor Organization (ILO) and the European Foundation for the Improvement of Life and Work constantly strive to monitor global trends in changing working conditions and service provision. For example, in 2019, the survey included approximately 1.2 billion workers in 187 countries whose exposure to shift work was assessed and compared. It turns out that between 10 and 30% of workers and employees perform intensive work and service activities at least once a month in night and day shifts. Changes in the circadian cycle cause what is called social jet lag, caused by changes in the nature of daily activities of Education, Work and Services. The „24/7" schedule in work and service activities is becoming dominant in modern society, whose members are required to work and serve around the clock and seven days a week. In the performance of military duties, in medical assistance, in military medical and emergency institutions, for workers in air, water and land transport and energy, on offshore oil platforms and geological exploration stations, in manufacturing, in the hotel business, a regime of work 24 hours a day.

Another foundation of our developments is the achievement of three authors in the discovery of the molecular mechanisms that control the circadian rhythm, for which they were awarded the Nobel Prize for Physiology or Medicine in 2017: Michael Rosbash, Jeffrey C. Hall, and Michael W. Young.

The circadian sleep-wake and fasting-eating cycles in eating behavior have a systematizing, synchronizing effect. In the active phase, when energy consumption is higher and food and water are consumed, the organs must be prepared for the reception, processing and absorption of nutrients. The activity of organs such as the stomach, liver, small intestine, pancreas and the blood supply to these organs requires internal synchronization, which can be provided by a internal clock [3]. During sleep, although energy expenditure and digestive processes are reduced, many important processes occur, including cell restoration, elimination of toxins, expression of pro-inflammatory cytokines, memory consolidation and information processing by the brain.

Experimentally, in the early 1970s, since circadian rhythms are associated with the light-dark cycle, structures were identified in the hypothalamus that receive direct projection from the retina of the eyes. The suprachiasmatic nucleus of the hypothalamus (SCN) receives extensive projections from the retina, and when the SCN is damaged, circadian rhythms are disrupted. 20 years later, the role of the SCN was confirmed by transplanting small grafts of neural tissue from the SCN region of a mutant hamster with a short 20-hour circadian period into non-mutant hamsters in which the own SCN was destroyed and the 24- hourly rhythm was abolished. Not only did the transplant restore circadian rhythms, but more importantly, the restored rhythms lasted for 20 hours, indicating that an important component of the clock – its period was transplanted along with the SCN [4].

The SCN in the human brain contains approximately 50,000 cellular circadian oscillators that are stable enough to generate circadian rhythms of neuronal firing for at least six weeks *in vitro*. This was first shown in dispersed SCN neurons of newborn rats placed in culture on a microelectrode array. Individual neurons exhibited robust circadian rhythms when electrically driven, but the phases of these individual rhythms differed, suggesting that SCN neurons act as individual clocks and that the underlying oscillations reside within individual cells rather than being a emergent property of a network of individual neurons [5, 6].

Transcriptional triggering is provided by two proteins called „Kaput circadian locomotor output loops” or, less tantalizingly, CLOCK (CLK), which are associated with the „brain muscle network” such as 1’ or BMAL1. The CLK-BMAL1 complex binds to E-box promoters, driving the transcription of five major clock genes, three Period (Per) genes, which give rise to PER1, PER2, and PER3 proteins, and two Cryptochrome (Cry) genes, which encode CRY1 and CRY2 proteins.

The SCN projects directly to about 35 brain regions, located mainly in the hypothalamus, and especially to those areas of the hypothalamus that regulate the release of hormones. Indeed, many hormones under the control of the pituitary gland, such as cortisol, are under a strict circadian regulation. In addition, the SCN regulates the activity of the autonomic nervous system, which acts to synchronize many aspects of physiology, including the sensitivity of target tissues to hormonal signals [7, 8].

The aim consists in testing an experimental model of desynchronization of the circadian rhythm caused by eating behavior and forced activity during the rest period and indirectly studying the interactions of the central oscillators of the hypothalamus.

Materials and methods

In our experimental model we used mature laboratory animals (rats) raised in a vivarium with a standard diet, with free access to water and natural light. Hedonistic foods, including favorite foods in the diet: egg yolk, pork, seeds, cottage cheese. An experimental animal model was used with the inclusion of 3 groups of laboratory animals (adult male rats) in the experiment: control (n=5); hedonic food during the rest period (08:00-16:00) (n=5); hedonic eating during periods of rest and increased physical activity at night. An animal model of „night work” was applied, based on forced activity in a rotating cage during daylight hours (in rodents the resting period). Forced motor activity of an animal during rest or sleep, for example. total sleep deprivation was simulated in a rotating cage with a diameter of 150 mm and a rotation speed of 12 rpm with a stop at 12:00 for food and water. The behavioral and physiological responses of the animals in this model are similar to those observed in night workers. To estimate vigilance during motivated feeding behavior, we determined the frequency of behavioral acts for the entire observation period (60 min, i.e. 3600 s), and calculated the total duration and average duration of each act. Concentration of attention was assessed by recording acts of searching and sniffing, approach to feeder, approach to drinker, acts of biting the cell, as well as the amount of food and water consumed during of registration. To estimate the emotional state, we recorded and estimated acts of care, relaxed sleep, as well as acts of expressing positive emotions, manifested in motor reactions in the area of the animal's head. The results of the evaluation of the food behavior indicator were systematically compared with the dynamics of body mass. To monitor locomotor activity during the circadian sleep-wake cycle, we placed and fixed an accelerometer (Actigraph, USA) on the back of an experimental animal, which allows non-invasive recording of motor activity during daily sleep-wake and fasting-eating cycles. Statistical analysis using ANOVA method.

Results

In the control group, during the rest period (sleep) during daylight hours on a standard diet, activity was 350 during meals and 150 units (according to the average actigraph indicators) after meals.

In the control group, during the period of activity in the dark with normal eating behavior and consumption of a standard diet, increased physical activity in the dark was detected within 800 units for every 2 hours.

The "Night work" model during the rest period (daylight hours) with hedonic food feeding led to significantly higher physical activity (Fig. 1).

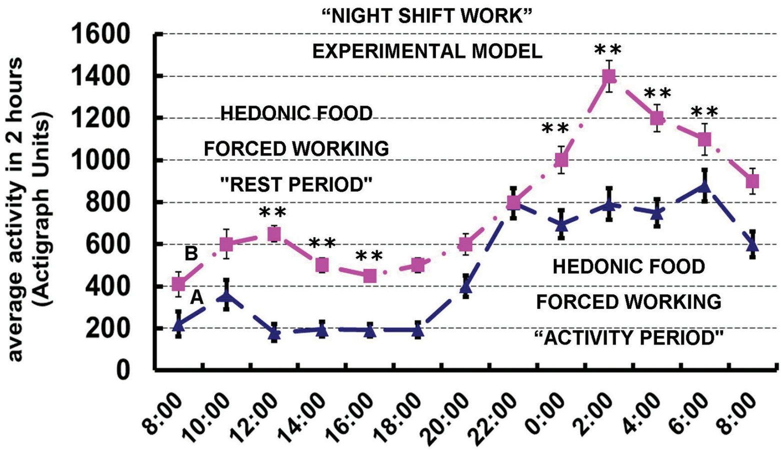

Figure 1. Average accelerometer recordings in the case of combining forced work and hedonic nutrition during the circadian cycle. A – control group; B – experimental group. ** - $P < 0.01$

The “Night shift work” model in the period of activity (dark time) in combination with hedonic nutrition caused a significantly higher physical activity up to 1400 ($P < 0.01$), and during the daylight hours physical activity tends to increase compared to physiological rest (Fig. 1).

Discussions

The complex interactions associated with sleep/wake generation are under normal conditions regulated by two endogenous factors called the homeostatic process (Process S), which is enhanced by wakefulness and the circadian process (Process C). This is a „dual-processor” sleep pattern. The circadian rhythm of promoting nighttime sleep and daytime wakefulness opposes a homeostatic driver that increasingly promotes sleep (S) during the day, and then during sleep the homeostatic sleep pressure dissipates toward the end of the sleep episode. The time of day most suitable for sleep - the „sleep window” - appears as a result of the combined influence of circadian and homeostatic factors. The sleep pressure in the sleep window will be the highest in the first half of the night, but it decreases gradually more so as the homeostatic drive to sleep dissipates towards the end of the night [9]. The changes we found in the emotional status of experimental animals are consistent with data obtained in a study of eating behavior using the Dutch Eating Behavior Questionnaire (DEBQ) in 24-hour working nurses in a major Emergency Hospital in Hong Kong. The result is obvious and indicates that round-the-clock duty determines the atypical nature of the circadian fasting-eating cycle, which is accompanied by the generation of negative emotions. Nurses who worked four or more shifts per month were more likely to have abnormal emotions and inhibition on the DEBQ [10]. It is important that when practicing disordered eating behavior, the risk of developing obesity and metabolic syndrome increases, even despite a low-calorie diet [11].

Conclusion

Under conditions of physiological rest under normal lighting conditions (from 08:00 to 22:00), with normal eating behavior and consumption of a standard diet, an increased physical activity in the dark is detected in the range of 800 units (according to average actigraph indicators) for every 2 hours. While during the day and during a standard meal, the activity is 350 during meals and 150 after meals. During the consumption of hedonic foods, motor activity according to actigraphic indicators was approximately 500-600, and in the dark the activity of was 700-800 units. Forced desynchronization during active period (in the dark) resulted in significantly