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## Consequences and management of sleep-wake rhythm disorders resulting from social jetlag and nightshifts

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## **Abstract**

Our day to night cycle is ruled by a social, biological and sun clock. The social clock being a local time is aligned with others' lives. The biological clock (circadian time) that controls our physiology and the sun clock that defines natural light and darkness. Social jetlag refers to the misalignment between local and circadian time. This term is usually used in reference to travels to places in different time zones. Nevertheless, it is worth noticing that "jetlag" also applies to people working in a medical industry such as doctors, nurses, paramedics, and others involved in an on-call work. Thus, I would like to look closer to the physiology of social jetlag and to analyze its implications.

**Keywords:** Social jetlag, circadian time, nightshift, melatonin, early chronotype, late chronotype, shift work disorder

## **Introduction**

Our day to night cycle is ruled by a social, biological and sun clock. The social clock being a local time is aligned with others' lives. The biological clock (circadian time) that controls our physiology and the sun clock that defines natural light and darkness. [1]

People have different timing of their sleep and activity which is often related to environmental changes and genetic variations. Some humans are so-called extreme early chronotypes while some are extremely late chronotypes. However, most of the population falls between these two extremes. Social aspects such as school and work can hamper with individual sleep preferences. The biggest problem seems to concern late chronotypes as they usually have a big sleep debt on workdays, for which they compensate on free days. This disparity, between work and free days, between local and circadian time, can be described as "social jetlag". [2] Nowadays, this term is mainly used in reference to travels to places in different time zones. Nevertheless, it is worth noticing that "jetlag" also applies to people working in a medical industry such as doctors, nurses, paramedics, and others involved in an on-call work. Night work, defined as a work shift lasting at least seven consecutive hours, which comprehends the interval between midnight and five o'clock in the morning, is nowadays very common and is still increasing. Between 10-30% of the workforce in the Western world work in this kind of manner. [3,4] Thus, I would like to look closer to the physiology of social jetlag and to analyze its implications to raise the awareness of significance of social jetlag consequences, especially among workers in a medical field.

## **Aim**

The aim of this paper is to provide a comprehensive review based on literature, concerning social jetlag and the consequences of nightshifts.

## **Materials and methods**

PubMed database and google scholar were searched for the following terms: "jetlag", "social jetlag", "nightshifts", "melatonin", "sleep" for the articles and written in the English language.

## **Physiology of sleep**

Pineal gland is an endocrine organ located in the posterior aspect of the cranial fossa and its primary function is to produce and secrete *N*-acetyl-5methoxy-tryptamine, also known as melatonin. [5] Renee Descartes described the pineal gland as the “Seat of the Soul”, as the main function of this structure is to receive and convey information about the current light-dark cycle from the environment through the production of melatonin cyclically at night (during dark period). [6,7,8] Melatonin can also be produced in other parts of the body such as skin, gastrointestinal tract, retina, bone marrow or placenta acting in an autocrine or paracrine manner. [9] Inner retina senses light and sends neural signals to the visual areas of the brain. However, a few retinal ganglion cells contain melanopsin and have an intrinsic photoreceptor capability that sends neural signals to non-visual areas of the brain, including the pineal gland. The photic information is further sent to the suprachiasmatic nucleus (SCN), the major rhythm-generating system in mammals, and from there to other hypothalamic areas. In case of a positive light signal, the SCN secretes gamma-amino butyric acid, which inhibits the neurons that synapse in the paraventricular nucleus (PVN) of the hypothalamus, consequently the signal to the pineal gland is interrupted and melatonin is not synthesized. On the other hand, in the darkness, the SCN secretes glutamate, which initiates transmission of the signal to the pineal gland. Nevertheless, it is worth noticing that constant darkness causes SCN to generate rhythmic output without light suppression, hence it is called an endogenous oscillator (master pacemaker or clock). [7]

## **Discussion**

### *Management of sleep-wake rhythm disorders*

Management of sleep-wake rhythm disorders is to readjust the circadian timing with the required sleep-wake period. Change of time zones and working during the night make it often impossible to avoid jetlag and consequences related to this. Some useful approaches to these sleep-wake rhythm disorders include taking melatonin, melatonin receptor agonists (agomelatine, tasimelteon) or light therapy. [10,11,12,13]

It is known that light exposure during the last hours of the usual sleep period moves the circadian rhythm forward (phase advanced). On the other hand, light exposure in the evening and in the first half of the usual sleep period moves the circadian rhythm back (phase delayed). [10]

Jetlag and nightshifts are perfect examples of sleep-wake rhythm disorders from an everyday life which often disturb normal functioning during the day. Jetlag is stronger in case of more time zones crossed and an easterly direction of travels, as it is more difficult to advance than delay the natural circadian cycle. [6,14,15]

In case of misalignment of the circadian rhythms due to jetlag, administration of 0,5-5mg of melatonin five hours before endogenous melatonin onset secretion and light exposure in the early morning have been proved to help in falling asleep earlier. [16] Daily dose of melatonin between 0,5mg and 5mg have similar effect, however people fall asleep faster and experience better quality of sleep after a bigger dose. More than 5mg of melatonin seem not to be more beneficial. [15] Because of not enough number of studies, there are no specific recommendations about melatonin intake for shift workers. [6]

#### *Jetlag and its effects on habits in different types of chronotypes*

Dr Till Roenneberg, et al. created the Munich ChronoType Questionnaire (MCTQ) which consists of a core module that is needed to determine chronotype of an examined person and some additional modules on lifestyle during workdays and free days, as well as the work details, time spent outdoors and stimulants such as cigarettes, alcohol, and caffeinated drinks. Since 2000, the MCTQ has been progressively optimized so that there are four different versions of them (MCTQ core, full, full children, shiftwork). [17]

Wittmann M. et al. conducted a survey with 501 volunteers who filled out the MCTQ as well as additional questionnaires on sleep quality, current psychological wellbeing, retrospective psychological wellbeing over the past week and consumption of stimulants. They found out that young people below 25 years old show the strongest correlation of chronotype, wellbeing and stimulant consumption. Additionally, late chronotypes of all ages have a higher cigarette consumption. These correlations are a consequence of social jetlag rather than a simple association to different chronotypes. [2] The results of this study suggest that jetlag strongly contributes to our lifestyles so as work (and school) schedules adapted to a certain chronotype would be very beneficial in the context of our habits.

#### *The impact of shift work on morbidity*

It is known that any kind of sleep disorders can lead to immune disruptions. The outcome of the study concerning sleep during the Covid-19 pandemic show that healthcare workers who were subjected to atypical workload and more nightshifts developed sleep disorders which was associated with work-related errors and Covid-19 infection susceptibility. [18]

According to a certain meta-analysis, shift work is associated with an increased risk of coronary events, acute myocardial infarctions, and ischemic stroke. However, shift work was not associated with overall mortality, or cardiac or cerebrovascular death. [19]

Skogstad et al. have recently conducted a 4-year follow-up study of shift workers and dayworkers in which they found an increase in pulse wave velocity (PWV) representing a possible increase of arterial stiffness, which is regarded as one of the earliest manifestations of vascular damage connected to increased risk of future cardiovascular disease, among the shift workers. [20,21]

Furthermore, Dasari et al. analyzed contribution of circadian rhythm disruption (CRD) to racial disparities in prostate cancer. The study suggests that CRD is one of the prostate cancer risk factors, and African American men have an increased susceptibility to develop CRD. [22]

#### *Sleep implications*

The American Academy of Sleep Medicine defines shift work disorder as a circadian rhythm sleep disorder and a primary sleep disorder. [23]

Vanttola et al. conducted a cross-sectional study regarding a prevalence of shift work disorder (SWD), among healthcare providers. Hospital workers without and with night shifts, as well as permanent night workers answered a survey on SWD and fatigue on their non-working days. The results show that prevalence of SWD was significantly higher among workers with nightshifts than among those without when using the cut-offs of  $\geq 1$ -3 non-day shifts. Employees experienced sleep disorders, sleepiness, physical and mental fatigue, depression resulting in poorer memory and decreased cognitive performance. The results also suggest that reliable cutoff for days with SWD symptoms is  $\geq 3$  per month which gives a 3%-6% of SWD. [24,25]

It is worth remembering about nurses who represent a particularly important group of healthcare providers, as they give 24-hour care in hospitals. A recent study involving shift nurses exhibits a higher incidence of mental health problems and burnout. [25]

#### *Lighting interventions*

Some studies show that lighting interventions are not very effective in reducing sleepiness among nightshift workers. [24,26-33] One of these studies investigated sleepiness among nurses during 3 consecutive nightshifts. It showed that bright light treatment reduces heavy

eyelids during night shifts as it delays circadian rhythm. However objective sleepiness measures are unaffected. Nor does light therapy reduced sleepiness during the day. [34] Nevertheless, Wu CJ et al. conducted a big systematic review and meta-analysis, including 14 studies, on effects of lighting interventions to improve sleepiness in night-shift workers. It showed that blue-enriched white light with a color temperature of minimum 5000 K was effective in improving the sleepiness of night-shift workers. So, it is highly recommended to use light treatment at the hospitals and other workplaces with shift work schedules. [24]

## **Conclusion**

“Social jetlag” is a broadly used term in a society and means the misalignment between local and circadian time. The possible causes of jetlag include travelling to different time zones and work schedules involving nightshifts. [2] It is important to be aware of inevitable consequences of sleep-wake rhythm disorders, such as change of habits, increased consumption of stimulants, increased risk of coronary events, greater Covid-19 infection susceptibility, a higher incidence of mental health problems or burnout. [2,18,18,25] Melatonin supplementation, light exposure in the early morning or light therapy are among useful approaches to jetlag, however there are no specific recommendations about melatonin intake for shift workers [6,16] Despite that, it was examined that blue-enriched white light with a color temperature of minimum 5000 K was effective in improving the sleepiness of people working during the night. [24]

## **List of abbreviations**

SCN - suprachiasmatic nucleus

PVN - paraventricular nucleus

MCTQ - Munich ChronoType Questionnaire

PWV - pulse wave velocity

SWD - shift work disorder

CRD - circadian rhythm disruption

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## Competing interests

The authors declare no competing interests.

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