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Review Article

Physiological Facets of Jet Lag: Melatonin is the Key Ruler

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ABSTRACT
It's the most exciting thing to move around from one section of the globe to the other part, swiftly. However, Jet lag is the most frustrating component of such long journeys. Jet lag happens when our internal clock is desynchronized by travelling across several time zones in a short time. Jet lag is not a badge of honour, but a significant modern problem. Hence, it's worth understanding the means to handle Jet lag without counting on sleeping pills. Melatonin has proven to be a better and safer treatment for Jet lag. This review is a general topic of interest and talks over the causes, and implications of Jet lag. It also gives special emphasis on the method to use judiciously timed exogenous melatonin to conquer the jet lag.
Key words: Melatonin, Jet lag, Circadian Rhythm, Pineal Gland, Time zone.

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INTRODUCTION

'I think a major element of jet lag is Nobody ever tells me what time it is at psychological home' - David Attenborough.

Tokyo, Japan is ready to host the Olympic Games, which is scheduled to be organized from July 2021 to August 2021. Athletes will travel from all over the planet to take part in the competition with a dream of winning a medal in their respective sports. Most of them have to travel across several time zones to reach Japan. For example, athletes from North America and Western Europe, when travel to Japan, face time zone variances of 8-11 hrs west and 6-8 hrs east respectively.[1]

Some athletes will travel to Japan a week before the commencement of competition and few reach Japan just a couple of days before the competition. In either case, athletes have to adjust to the new Time zone as quickly as possible so that they are mentally and physically well-prepared to give their best in the competition and participate with high-intensity to make their nation proud. But those who have travelled across many time belts in quick succession are going to suffer from Jet lag. Jet lag might become a vault between the athletes and their dream medal. So, let's help such athletes to accomplish their dream.

Jet Lag: Rift between Internal and External Clock

Jet lag is one of the frustrating parts of travel. Jet lag ensues when a person passes over many zones in a short period, disrupting his circadian rhythm. Nobody desires to pay his or her vacation wired within the dark and yawning throughout the days[2] (Figure 1). Jet lag happens once your biological time, conjointly referred to your internal clock is thrown off by move across many time zones.[3] Once the time of day you are experiencing doesn't jive in conjunction with your internal clock, your body system gets confused. Your body is telling you that it's time to sleep however, outside the sun is rising.[4] Jet lag isn't a badge of honour, which would make travellers feel proud. Instead, it's a significant modern problem. It has a widespread effect on everything from weight gain to manic disorder.[5] However, it's additionally a tough reality of contemporary life. It might be not possible to develop jet lag when travelling by boat, horse, cart, foot, etc., in which our speed of travelling is slow.[6] Hence, the body would have enough time to regulate civil time once motion through a neighbourhood.

In step with Medical News Today, the term, 'Jet lag' may be a relatively new one; because 80 years ago, nobody cosmopolitan across many time zones quickly as there was no jets or the opposite fairly speedy transportation. For this reason, many languages, similar to Spanish or German conjointly use English term Jet lag in their traditional languages.

Jet Lag vs Travel Fatigue

Physiological and physical performance variables are affected following travel across multiple time-zones. Jet lag additionally referred to as 'Desynchronises' or 'circadian dysrhythmia' is temporary, but it can interfere with our activities in many ways. Aviation across many time zones through trans meridian flight causes many problems. A number of these problems occur during the journey in the flight, and a few of them transpire within the days after landing a new location, with a different time zone.[7] Fortuitously, these negative effects are collectively referred to as 'jet lag', but they are truly

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two different entities and phenomena; travel fatigue and jet lag. Each has its source and effects. Travel fatigue attributes the group of symptoms that occur or straightaway after long flights. These symptoms embody perplexity, weariness, and headaches. These problems are usually a source of the discomfort associated with being in an aircraft within a confined space restricted to your seats, dehydration, sleep loss, low atmospheric pressure, low hardness, etc., for 5-10 hrs. In distinction, Jet lag is the cluster of manifestations that occur in the days after aviation, across many time zones.[8] These symptoms embody daytime sleepiness, the issue of sleeping in the dark, headache, irritability, poor mental, and physical performance, and weak digestive tract function. These symptoms are fundamentally a result of the discrepancy between the circadian rhythm and the environmental clock. Our sleep and wake cycle is regulated through circadian rhythm that signals our body, when to remain awake, and when to fall asleep.[9] Our body's clock continues to be synced to our original time zone, rather than the new geographical zone which is our destination. The outcome of this rift between internal and external clock is nothing but Jet lag.[10]

Throughout the resynchronization period, internal rhythms are out of the path with the external surroundings, leading to the complaints of poor sleep, alertness, performance than on. The direction you're flying will have an enormous impact on your weariness symptoms too. Manifestation tends to be additional severe once moving eastward. That's as an outcome of staying awake later to assist your body accommodates a new geographical zone is less complicated than forcing your body to go to sleep earlier.[11] The maximum geographical zone shift that causes Jet lag is twelve hours. If time zone shift is more than twelve hours, for instance, 20 hrs, then we have to subtract it from 24 i.e. (24-20=4) here the time zone shift is 4 hrs, but in the opposite direction.

Jet Lag: Complications

Jet lag afflicts tens of thousands of individuals annually and the effects of jet lag on human performance, while generally are ephemeral, nevertheless can have a huge impact on commerce, government, and even the outcome of skilled sports contests. Thus, athletes competing in the Olympics might have to lose their medal even though they are capable of winning it, just because of jet lag.[12] Frequent jet travel has long-term health risks. Psychological feature deficits, lobe atrophy, as determined by magnetic resonance imaging scans and disturbances within the menstrual cycle will all occur with frequent jet travel. Following trans meridian travel, it's possible that meals are going to be ingested at the inappropriate circadian phases and recurrent occurrence of this might increase the chance of upset and type II polymeric disease. There's a magnified risk of cancer on the wing attendants who often fly across many time zones. Studies in mice have shown that chronic jet lag accelerates the event of malignant tumours and reduces survival time. Finally, old mice subjected to weekly half-dozen hour part shifts within the light-dark (LD) cycle died sooner once the LD cycle was advanced (equivalent to visit east across half-dozen time zones) than once it had been delayed (trips west) and each team died before the controls who were not shifted.[13] Thus, the results of Jet lag, each short and long are a public health issue that requires to be addressed and there's a requirement to prevent or a minimum of minimizing it. If you don't take any measures, your circadian rhythm adapts slowly to abrupt phase shift. Hence, to overcome jet lag briskly, one of the safest ways out is exogenous melatonin.

Melatonin: Opens the Sleep Gate

Melatonin is an endocrine hormone, secreted from the Pineal gland. The Pineal gland weighs approx. 120 mg and lies between the superior colliculi, i.e. roof of the ventricle at the posterior end of the corpus callosum. It's got a very rich blood supply. It is additionally referred to as 'Neuroendocrine transducer' because it forms and secretes a hormone in response to sympathetic activity. The pineal gland is large in infants, begins to reduce in size, and calcifies during the second decade of life, however, continues to secrete hormones. It contains a high quantity of 5- hydroxytryptamine (serotonin), monoamine neurotransmitters (nor epinephrine), and hormone (melatonin).

The hormone is secreted rapidly into the CSF and blood. Being extremely lipid-soluble, it penetrates the cells in neural structure, hypothalamus, midbrain, peripheral nerve fibres, and gonads (Figure 2). Melatonin considered as "the light of night" is secreted from the ductless Pineal gland, chiefly in the dark.[14]

The hormone is concerned with sleep regulation, as well as a very range of alternative cyclic bodily activities, and circadian rhythm in humans. Melatonin is exclusively involved in signalling the 'time of the day' and 'time of the year', considered assisting each clock and calendar functions to all tissues and therefore regarded as, body's chronological pacemaker or 'Zeitgeber'.[15]

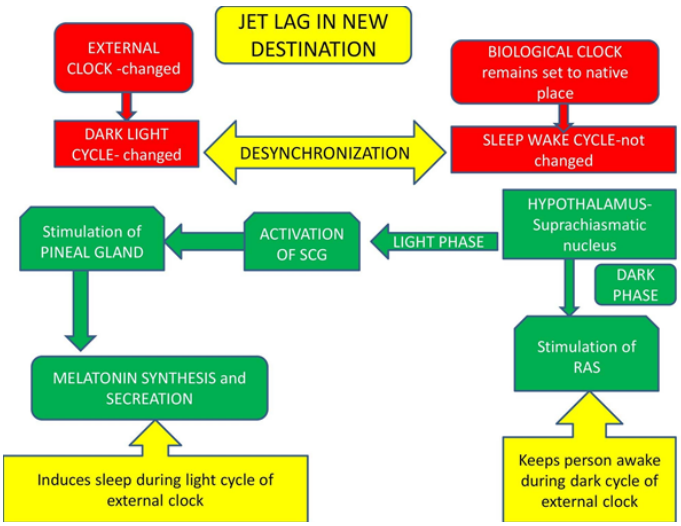

Figure 1: Jet Lag.

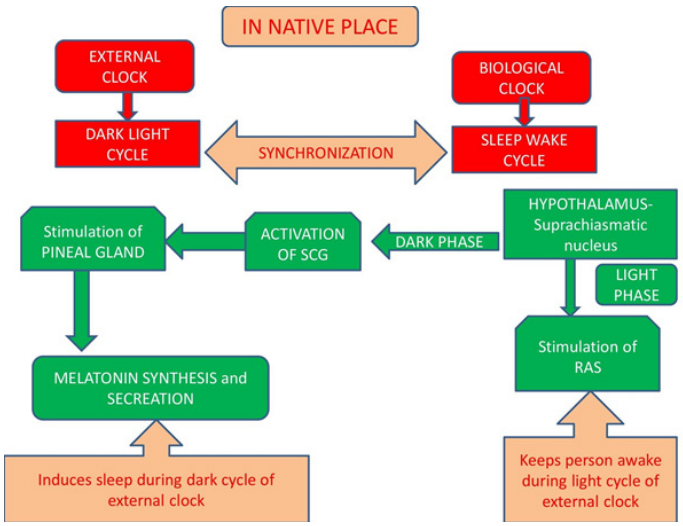

Figure 2: Normal circadian rhythm (SCN-superior cervical ganglion).

Endocrinology of Melatonin

Light signals from the retinal tissue layer project to the pineal gland via the Suprachiasmatic Nucleus (SCN), a chief nucleus of the hypothalamus and sympathetic nervous system. Throughout sunlight hours, photo signals hyper polarize the receptors of the retina, which inhibits the production of norepinephrine.[16] The inhibitory effect of light on the release of norepinephrine is withdrawn with the onset of darkness. Thus now, norepinephrine is released which activates the system. There will be Number and varieties of alpha 1- and beta 1-adrenergic receptors within the Pineal gland. The enzyme 'arylalkylamine N-acetyltransferase' is activated which is the catalyst of the rate-limiting step of melatonin synthesis. Thus, the rate of hormone synthesis is magnified, and there will be the release of the Melatonin and it enters the blood through passive diffusion. The temporary arrangement of the human sleep/wake and circadian systems are related in such a way that the assembly of endogenous hormone begins two hours before the habitual time of day. The daily minimum of the core body temperature rhythm (CBT min), that coincides with the daily low-point of the circadian cycle, happens seven hours after onset of melatonin discharge.[17]

The daily peak of the core body temperature rhythm (CBT max), which coincides with the daily high-point of the circadian cycle, occurs 12 hrs after CBT min. Therefore, an individual who ordinarily sleeps from 23:00 to 07:00 can have hormone on set at 21:00, CBT min at 04:00 and CBT max at 16:00.[18]

Melatonin Works in Conjunction with Our Body's Biological Time.

Melatonin levels begin to raise your body once, it's dark outside; signalling for your body that it's time to sleep. It additionally binds to receptors in the body and may assist you to relax. As an example, the hormone binds to receptors within the brain and facilitates to cut back the nerve activity. Within the eyes, it can facilitate to reduce dopamine levels, a hormone that helps you to stay alert. The largest temporary state, and the poorest mental/physical performance, occurs in 2–3, hrs either facet of CBT min, equally, the largest alertness, and greatest mental/physical performance, happens within the 2–3 h either side of CBT max.[19]

Role of Melatonin in Jet Lag

Inceptive exploration of rats whose pineal gland was surgically removed showed a diminutive effect on sleep-wake cycles.[20] These facts are strengthened by a recent study, which indicates that eradication of the Pineal gland has no impact on the sleep of rats. Nevertheless, if these species without pineal glands when subjected to an instantaneous time shift (as jet lag), they customized expeditiously to the new schedule. This observation instructed that the Pineal gland, and by inference melatonin, decelerates the adoption of these species to the new zone, being undesirable in very natural surroundings.[21]

This prospect is fortified by the fact that the seduction of hormone discharge by the beta-blocker atenolol out-turns in swift adaptation to light-induced phase- shifts in humans. Sarcastically, while exogenous melatonin is utilized to expedite adaptation, it's feasible that endogenous production performs is to try to do the opposite.[22]

The apparent solution to jet lag is Chronobiotic - a drug that shifts all circadian rhythms within the desired direction and acts as a Zeitgeber to take care of stable part, once the latter is obtained. Since Melatonin originally was envisioned as a 'human chronobiotic' in 1983, its phase-shifting and, to some extent, abusive properties have been investigated extensively in conjunction with its acute effects on sleep, temperature, and performance.[23,24] Thus, exogenous melatonin is needed to synchronize with the new place (Figure 3).

A Standard Prescription of Melatonin Tablet for Jet Lag

You might be thinking, "When and how to take the melatonin tablets?" You will get all the information regarding this in the text. The current

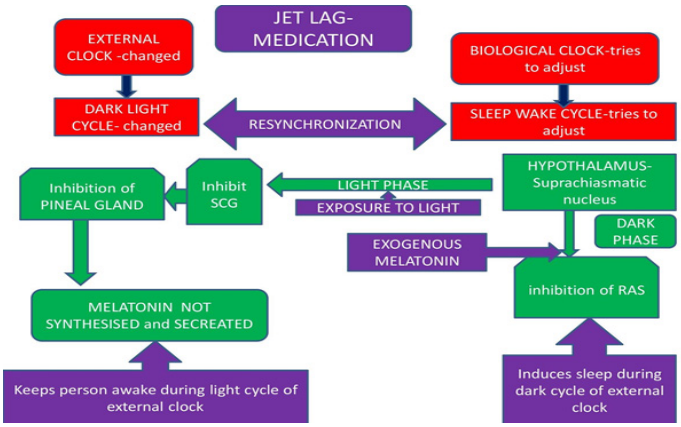

Figure 3: Melatonin is the safest option to overcome Jet lag.

texts specify the timing of daily administration of exogenous melatonin to overcome jet lag. When travelling east, you actually fall inside a phase advance window. You can take one pre-flight tablet in the late afternoon on the day of departure and post flight tablet for 4 days at bedtime of your new place. When going west (phase delay), you can take melatonin tablets post-flight for 4 days. No pre-flight treatment is given for westward flight.[25]

According to one of the researchers, eight out of ten trials found that melatonin when taken at the bedtime of the target destination, adapted very quickly compared to controls. In one of the experiments, people with jet lag where divided into two groups. One was treated with melatonin and the other with placebo. Sleepy during daytime, sleep latency and fatigue was reduced in the group with melatonin than the group who were given placebo. Sleep quality during the night and recovery were greatest in the group of people who were treated with.[26]

Physiology of Exogenous Melatonin for Jet Lag

Exogenous melatonin appears to act through a combination of acute effects. Exogenous melatonin taken just before local bedtime induces synthesis of endogenous melatonin (Figure 4). Exogenous melatonin hastens the conversion of tryptophan to melatonin, helps in resynchronization between external and internal clock.[25] Adults, 0.5-10 mg of melatonin taken at bedtime of your new place relaxes and lowers your body's physiological mechanisms.[27] It lowers your alertness, increases sleepiness, reduces body temperature, etc. It is believed to reinforce physiology and behaviour associated with darkness and phase shifts. Thus, help in adapting to phase shifts. Melatonin in jet lag is considered as the safest application of melatonin.[28]

Special Precautions and Warnings

One should avoid taking melatonin during pregnancy or breastfeeding; have an autoimmune disease, a seizure, and if in depression. Melatonin also has some possible drug interactions. Doctors should be consulted before using melatonin if any of the following has been taken: blood pressure medications, blood thinners, anti-depressant, diabetes medications, anticoagulants, anticonvulsants, immunosuppressant drugs, the medication fluvoxamine (Luvox), a selective serotonin reuptake inhibitor (SSRI), and medications. One should also avoid taking melatonin with alcohol. If you're travelling for a vital event, bear in mind to arrive a day or 2 earlier so, you'll properly accommodate your new geographical zone. Gradually adapt to your new schedule before your departure by attending to bed an hour earlier or later than traditional every evening, looking at the direction you're travelling. Take care that you're well-rested before your travels. Being sleep-deprived to start with will exacerbate weariness. In-flight, keep yourself hydrous.

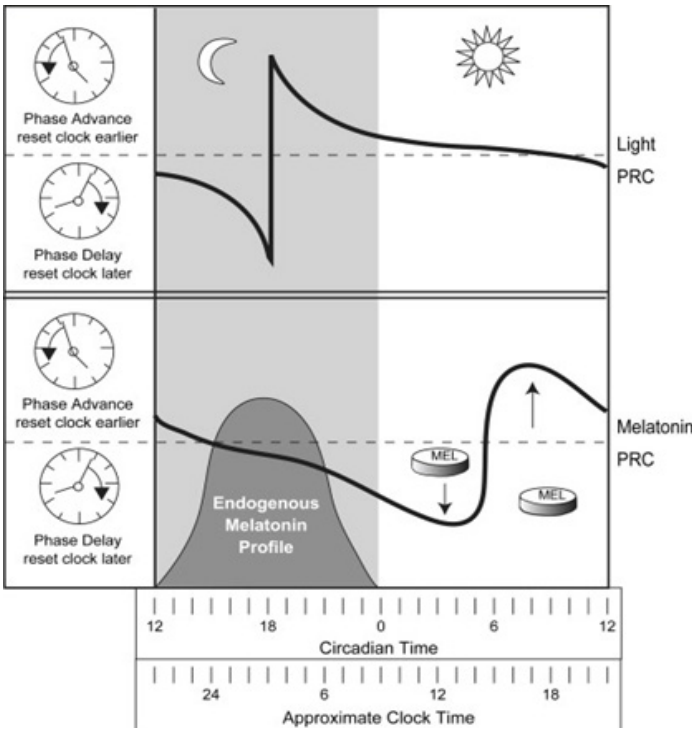

Figure 4: Exogenous melatonin to increase desynchronization but endogenous melatonin to resynchronize to new local time.

Dehydration will make the symptoms of jet lag worse. Limit your caffeine and alcohol consumption. They both increase the need to urinate, which may disrupt the sleep and may aggravate the symptoms of Jet lag. After arrival, remain on new schedule. Try to head to bed at a time that will be traditional for that time zone, despite however tired, you will feel. Take into account setting an alarm within the morning so, you don't sleep too late. Natural light is one of a foremost necessary component of resetting sleeping and waking cycle. Exposing yourself to morning light will assist you to adapt travelling eastward, whereas, exposing yourself to evening light will facilitate travelling westward.

CONCLUSION

Even though jet lag is a great challenge to handle, the above article suggests many ways to deal with jet lag. Judiciously timed exogenous melatonin intake has proven to be an optimum and an adequate solution to deal with the Jet lag. Following all the precautions, Olympic athletes can use melatonin to fight against Jet lag. It should be noted that people disagree greatly within the expertise of jet lag, with some travellers extraordinarily affected, whereas, others who could have flown the same route could report no weariness symptoms. This means that individual variations could powerfully influence the effectiveness of melatonin. Melatonin's side effects should not be neglected because it will cause some safety issues with a few folks. Invariably make it a point to consult doctor before beginning the course of melatonin because it will interfere together with your alternative medications. Besides taking special precautions, it's timings and dosage being additionally (crucial) than the rest. Hence, the exogenous hormone should be taken with exactitude.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ABBREVIATIONS

SCN: Suprachiasmatic nucleus; **SCG:** Superior Cervical Ganglia; **SSRI:** Selective serotonin reuptake inhibitor.

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