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Jet lag: symptoms, causation and minimization

Review

Jet lag is a misalignment of the human circadian rhythm which is regulated by the suprachiasmatic nucleus in the brain and caused by crossing time zones too fast for the biological clock to keep up. Main symptoms are intense sleepiness or insomnia at inappropriate times. Other symptoms are cognitive impairments, altered digestive functions or depressive symptoms. There is no aid to entirely avoid jet lag, but there are ways to minimize the symptoms, such as phase-advancing or delaying the circadian rhythm before a flight with help of exposure or avoidance of bright light, melatonin and pre-adjusting the sleep schedule. The same resources can be used after arrival to reduce the symptoms. However, many different factors have an influence on the development of jet lag. More research is needed to gain a better understanding of how these are related to each other in detail. The findings are relevant for travelers and traveling workers and shift workers in order to be able to carry out their professional and social activities without the hindrance of jet lag.

Keywords: sleep, jet lag, melatonin, light, biological clock, circadian rhythm

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INTRODUCTION

Jet lag is the set of symptoms that results from a misalignment of the biological clock due to the rapid crossing of time zones to the east or west, shift-work or blindness. These are categorized as 'disorders of entrainment' (Moore, 1997). Entrainment is the process of resetting the internal clock to the external 24-hour rhythm. The human body is used to a certain cycle of light and dark and therefore a certain wake-and-sleep cycle. This cycle is also known as circadian rhythm: physical, mental and behavioral changes that follow a roughly 24-hour cycle, responding primarily to light and darkness in the environment (Moore, 1997). The name is derived from Latin, where circa means about and diem means day. When this cycle is disrupted suddenly or changed significantly by flying over several time zones, it takes some time for the body to reset this rhythm to the new local time. The resetting of the sleep-and-wake cycle takes a few days and usually brings about some behavioral symptoms. The main symptoms experienced when having jet lag are (intense) sleepiness or sleeplessness at unusual times, depending on whether the flight was westward or eastward (Arendt, 2009; Sack, 2009).

Several questions still arise around jet lag. For instance, it is unclear why certain people do suffer a lot from jet lag while others hardly experience any symptoms. This could be due to individual differences such as age, frequent flying, or the flying circumstances, like direction and number of crossed time zones. Additionally, there is evidence that flying to the west results in few, or even no, jet lag symptoms (Eastman & Burgess, 2009; Haimov & Arendt, 1999; Kalat, 2010; Sack, 2009). However, anecdotal evidence and personal experience suggest that when traveling westward and crossing multiple time zones, there can be quite strong symptoms, like intense daytime drowsiness and waking up very early in the morning, even when going to sleep late.

The answers to these questions and contradictions are beneficial to athletes, aircraft staff, shift-workers and business personnel. If they suffer less from jet lag, they will perform better and suffer less. They could save time by avoiding or minimizing jet lag in advance instead of going a week early to recover from the jet lag on time. The same counts for other passengers who travel through time zones, they do not have to be impaired by jet lag symptoms to perform their daily activities.

This literature review will explain what exactly jet lag is, which factors can alleviate jet lag symptoms and whether jet lag can be avoided. To acquire a better understanding of jet lag and its cause(s), the brain, the biological clock and hormone mechanisms involved in it need to be examined and described. So do the different factors that can contribute to jet lag. Finally, possible approaches for symptoms or jet lag alleviation will be considered. These are medications, staying up until local sleeping time or pre-advancing or -delaying the circadian rhythm and bright light.

METHODS

To address the above mentioned issues and questions, we searched PsycInfo (EBSCO) and started with a broad search term. The first search criterion was "jet lag" and returned 232 hits. To make this search more specific, we changed the criteria to "jet lag" in the "title", this returned 61 hits. For a general description of jet lag and to find information about the possible treatments, 11 articles were carefully selected. These 11 were selected by reading the titles and selecting those that were not too specific. The remaining articles were not investigated due to limited access (other search networks) or because they were just short reviews. Another search criteria was "jet lag and melatonin", the useful articles were the same articles as found with the criteria "jet lag" only in the title. For the more specific matters like jet lag in the elderly and in frequent travelers like air cabin crew, we used Google Scholar and selected articles by the relevant titles.

WHAT IS JET LAG?

When traveling through two or more time zones our biological clock becomes disrupted. Crossing two or less hardly affects individuals (Auger & Morgenthaler, 2009). In this situation we call it jet lag, but the behavioral symptoms related to it also occur in shift-workers. In both cases, the internal clock has to realign to the new circadian rhythm since it is adjusted set to other sleep-and-wake rhythms. It takes some time for the biological clock to reset, hence internal or endogenous signals for sleeping and waking might not match with the local periods of light and darkness (exogenous rhythms). Endogenous rhythms are internally driven (i.e. body temperature), and exogenous rhythms which are driven by an external influence or environmental cue, like light. Usually resetting the rhythm takes about one day for each hour of time zone that is crossed (Haimov & Arendt, 1999).

Typical jet lag symptoms are daytime drowsiness, insomnia and general fatigue. Additionally, depressed mood, cognitive impairment like loss of motivation and concentration, loss of appetite, altered digestive functions, diarrhea and decreased physical performance can occur (Waterhouse et al., 2002) . For most people, the symptoms are worse and they have more difficulties with readjusting when traveling eastward than westward (Arendt, 2009; Srinivasan, Spence, Pandi-Perumal, Trakht, & Cardinali, 2008). Going east, your circadian rhythm gets phase advanced. This means shortening the day, since you fly forward in time. Going west, the circadian rhythm gets phase delayed (Paul et al., 2009). The day becomes longer, because you fly back in time, which is comparable to staying up longer than usual. It is easier to sleep after being awake longer than usual compared to going to sleep earlier before your body's 'sleeping time', because the endogenous period of the body clock is on average a bit longer than 24 hours in the absence of external feedback (Moore, 1997; Schulz & Steimer, 2009). This is also called the free-running period. Taking this into consideration, there seem to be differences in jet lag symptoms after flying eastward or westward. Advancing (after a westward flight) or delaying (after an eastward flight) the circadian rhythm brings about different symptoms. These are intense sleepiness and waking earlier than usual, or, after an eastbound flight, insomnia during local nighttime and drowsiness during the day.

THE BIOLOGICAL CLOCK

The operation of the biological clock starts in the brain, with light entering the eye and causing a cascade of events as shown in figure 1. The results of these events are, amongst others, our circadian, or daily, and circannium rhythms.

Circannium rhythms are our ‘seasonal’ rhythms. They are more present in animals, for example, they are present for helping birds to know when to fly south before the winter and migrate back north in spring (Kalat, 2010). These rhythms are generated by endogenous pacemakers, the suprachiasmatic nucleus (SCN) in this case. The SCN is located in the brain just above the optic chiasm and lateral to the third ventricle in the anterior hypothalamus. Its primary function is to generate and regulate circadian rhythms. To generate these circadian rhythms, the SCN uses information of light and dark. However, also without that environmental feedback the SCN can generate circadian rhythms (Klein, Moore, & Reppert, 1991).

Circadian rhythms run for approximately 24 hours, usually a little longer than 24 hours in humans (Schulz & Steimer, 2009). Therefore these endogenous rhythms need exogenous feedback to run in 24-hour cycles: a “Zeitgeber”, the German word for time provider or determiner. Zeitgeber can be meals and temperature of the environment. At daytime for example, the environmental temperature is higher than at night time. The most important Zeitgeber however, is the light-dark cycle of the day. A recent study suggests that light not only regulates the biological clock, but also cognitive brain functioning (Gaggioni, Maquet, Schmidt, Dijk, & Vandewalle, 2014). To receive this light-dark feedback, a connection between the visual information system and the pacemaker is necessary. The SCN gets this feedback through the retino-hypothalamic pathway. This pathway is the connection from the retina to the SCN and integrates light information with the endogenous cycle, as seen in figure 1 (Isobe & Nishino, 2004; Moore, 1982, 1997). Light perceived through the retina is transmitted through this pathway to the SCN, where the latter controls the pineal gland via the paraventricular nucleus (Isobe & Nishino, 2004). The pineal gland is a small endocrine gland located between the two hemispheres and attached to the third ventricle, posterior to the thalamus (Moore, 1982, 1997). The pineal gland is responsible for melatonin secretion, the ‘sleeping hormone’. Melatonin secretion starts a few hours before bedtime. When it becomes dark (evening/night), melatonin is secreted, as light causes suppression of melatonin secretion. This effect is especially pronounced with sun light, although very strong artificial light can cause a similar effect (Lewy, 1983).

Melatonin influences circadian and circannium rhythms. Once those rhythms are set, it is difficult to reset them. After crossing time zones, the inner clock is still set to the ‘old’ light-dark cycle, thus the endogenous signals do not match with the new exogenous cycle. The inner clock has to reset, this happens slowly. The collection of symptoms caused by this inner clock reset is what we call jet lag (Kalat, 2010; Sack, 2010).

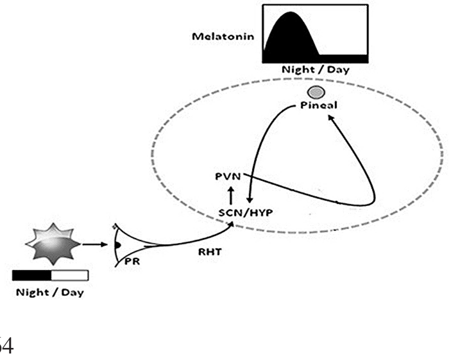

Figure 1: Light is perceived through the retinal photoreceptors (PR) and transmitted through the retino-hypothalamic tract (RHT) to the SCN in the anterior hypothalamus (HYP). The SCN regulates melatonin release from the pineal grand via the paraventricular nucleus (PVN) (Isobe & Nishino, 2004; figure adapted from: http://www.photobiology.info/Tosini.html).

Another factor contributing to the working of our biological clock is the synchronization of circadian rhythm and body temperature. Our body temperature is synchronized to our circadian rhythm, when it is sleeping time the temperature drops. Between 3 and 7 a.m., it is at its lowest. When the core temperature is dropping strongly or when it is at its lowest, it is the easiest to fall asleep. Usually that is at night time, but when jet lagged, the old night time is not the current, so body temperature drops at day time, which makes us sleepy, or it rises at night time, which causes trouble with falling or staying asleep (Waterhouse, Reilly, Atkinson, & Edwards, 2007).

FACTORS INFLUENCING JET LAG

As discussed earlier, when flying westward, we fly back in time. Most likely, sleepiness in the afternoon or early evening and waking up early in the morning will occur, since the 'new morning' is the old noon. When flying eastward, we fly forward in time, which means a few hours of the day are skipped. This results in insomnia at night and waking up late, since one falls asleep later. A study by Lemmer, Kern, Nold, and Lohrer (2002) measured several functions in top athletes after a westbound flight over six time zones (Frankfurt to Atlanta) and an eastbound flight over eight time zones (Munich to Osaka). Several functions including jet lag symptoms were measured. Jet lag symptoms remained until the 5th or 6th day after the westbound flight, and until the 7th day after the eastbound flight. The symptoms after flying east seem to last longer than after flying west, assuming the difference of two time zones is not significant.

The above results do not indicate conclusively that it takes longer to reset the circadian clock after an eastward than after a westward flight, since there is a difference in flight duration and number of crossed time zones (Lemmer et al., 2002). A more plausible explanation for the difference in realignment time is the free-running period of the biological clock. Since we have this natural tendency to prolong our day every day a little bit, it is easier to phase delay the circadian rhythm than to phase advance it (Auger & Morgenthaler, 2009; Eastman & Burgess, 2009; Sack, 2010; Waterhouse et al., 2002). Regarding this data, eastward time zone crossing seems to be harder to recover from due to the more persistent jet lag symptoms and the harder to overcome phase advance, which is likely a result of the free-running period. As the symptoms differ for each direction, different directions might require different treatment strategies.

Nonetheless, travel direction is not the only factor that can contribute to jet lag. Flight duration, how many time zones have been crossed and age of the traveler seem to make a difference in ability to cope with jet lag as well. Flight duration (when flying east- or westward) and number of time zones crossed have similar effects, since increased flight duration (east- or westward) usually results in an increased number of crossed time zones, or the other way around. The severity of jet lag increases when number of crossed time zones increases. Severity here means the symptoms last longer and can be more intense due to the fact that the circadian rhythm needs more time to readjust to bigger time differences. Lemmer et al. (2002) support this. However, further research should explore whether the difference in more or less severe jet lag experience is due to crossing more time zones or due to different flight directions.

With respect to age effects, Monk, Buysse, Reynolds, and Kupfer (1993) conducted a research where they induced jet lag in elderly people (aged 71 – 91 years) by making them adjust to a 6-hour phase advance. The study was done only with advancing the rhythm, no data was found about a phase delay. They compared the outcomes from participants in their study to the outcomes of younger participants (aged 37-52) from a similar study (Monk, Moline, & Graeber, 1988). The older half seemed to adjust the timing of their circadian temperature rhythm better to the new circadian rhythm than the younger half. On the other hand, the older people seemed to have longer enduring sleep disruption and daytime sleepiness than the younger subjects. In agreement with the latter results, Auger and Morgenthaler (2009) shortly describe a simulated jet lag study. Middle aged subjects (37 – 52 years) and young subjects (18 -25 years) took part in the study. The simulation required a 6-hour phase advance, comparable to an eastward flight where you cross six time zones. The older subjects had more problems with continuous sleeping afterwards, they experienced more interruptions in their sleep and also showed greater impairments in day time alertness. This suggests that with increasing age, there might be more difficulties with coping with jet lag, at least concerning sleepiness. This might be due to the fact that older travelers have more rigid habits and therefore might have more trouble adjusting their biological clock (Eastman & Burgess, 2009; Waterhouse et al., 2002). However, it is rather complicated to draw a conclusion out of the results of the two studies. They are hard to compare because they are about four different age groups between which there might be many differences not controlled for.

Moreover, Waterhouse et al. (2002) found results that make the previous suggestions even more inconclusive. Older subjects suffered less from jet lag and fatigue than the younger subjects who participated in the study. They seem to be more eligible to “pace themselves” than younger people. Cooper (2006) mentions that a few studies and surveys showed that older people might have more trouble with fatigue due to long walks through the airport, stress and carrying luggage than their younger fellows, but that they suffer less from jet lag than younger travelers. Thus, even though it is said that elderly people have more trouble with jet lag symptoms, we cannot draw that conclusion from above mentioned studies since they are quite contradictory.

Special care has to be taken with phase advancing the inner clock, as one has to take a few things into account to not make the advancing work the other way around. One thing for example is if an ‘early bird’ or a ‘night owl’, people who are more morning or night active respectively, wants to advance the rhythm. It is harder for a ‘night owl’ to be inactive early in the night than for an ‘early bird’. Moreover, it would be even better for a ‘night owl’ to delay the phase instead of advancing it, but this also depends on the number of time zones crossed, the desired sleep schedule at the destination and when the person is the most active (morning or evening). The more time zones are going to be crossed, the more beneficial it is for a night owl to delay instead of advance the circadian clock (Eastman & Burgess, 2009).

HOW TO MINIMIZE JET LAG

There are several methods and moments to do something about jet lag. Suggested approaches are bright light treatment, melatonin treatment, pre-adjusting the circadian rhythm, taking departure and arrival times into account or simply 'ignoring' the jet lag and sticking to the local social agenda (Paul et al., 2009). It all comes down to shifting the biological clock as fast as possible to the new time.

Before the flight, circadian rhythms can be advanced or delayed, depending on flight direction. This can be done by going to sleep earlier or later for eastward of westward traveling respectively, in combination with melatonin intake and/or light treatment. The same methods can be used after the arrival, to adjust faster to the local time and light-dark cycles.

When traveling eastward, it is the most helpful to advance the biological clock. This can be done by gradually advancing the time of going to sleep one hour each day and being exposed to bright light straight after waking up. Advancing two hours per day would be too much because it is too fast for the circadian rhythm to adjust (Eastman, Gazda, Burgess, Crowley, & Fogg, 2005). Advancing sleep time can be done by taking melatonin in the evening on the days before the departure (Waterhouse et al., 2007), or increasing the melatonin secretion naturally by staying in dim light. The closer the phase advance before the flight is to the number of time zones to be crossed, the less the circadian clock has to adjust after the flight, and the less one will suffer from jet lag symptoms, hence the less severe will be the jet lag (Eastman et al., 2005). Advancing or delaying the circadian clock before traveling also shifts the moment of the minimum body temperature, which is of big importance when trying to sleep since it helps to initiate and maintain sleep (Eastman & Burgess, 2009).

When traveling westward, the most appropriate approach is delaying the sleeping time combined with bright light exposure in the evening (Sack, 2009). Light is the primary cue for entrainment of the circadian clock, therefore it is of high value to work with bright light when advancing or delaying sleeping schedules (Sack, 2009). This is confirmed by Eastman and Burgess (2009), who describe how melatonin, bright light and sleep schedules can be used to avoid or minimize jet lag. To delay the circadian rhythm before going westward, the best way to do so is exposure to bright light one to two hours before going to sleep and gradually increasing that a few days before the actual flight. Additionally, in combination with the light, going to bed later than usual is of big importance. After waking up, bright light should be avoided. This can be done by sleeping in a dark room, wearing an eye mask when sleeping or wearing sun glasses or something similar when going outside. Nevertheless, even in controlled laboratory studies there are individual differences in how much the phases shift following exposure to bright light (Eastman & Burgess, 2009).

Phase advancing or delaying circadian rhythms before the journey is started, will also shift the moment of the minimum body temperature, which helps initiating and maintaining sleep. Paul et al. (2009) investigated phase delaying and advancing circadian rhythms with exposure to bright light and the results showed that there were significant phase changes after the treatment. In another study on pre-shifting the circadian rhythm (Eastman et al., 2005), subjects gradually advanced their rhythm with bright light exposure three days before an eastward flight. This showed that advancing circadian rhythms can be used before an eastward flight to reduce jet lag.

To help minimizing jet lag during the flight, sleep should only happen during destination sleep time. It is helpful to use melatonin to facilitate sleeping while being on board (Samuels, 2012). Furthermore, it is important to get as comfortable as possible and to drink plenty of water to avoid dehydration because of the dry cabin air. This can help avoiding or minimizing travel fatigue, but not the actual jet lag symptoms (Haimov & Arendt, 1999). It is important not to confuse the two: jet lag is the result of adaptations that occur when the body has to adjust to a new time zone or a new circadian rhythm. It takes a few days and consists mainly of fatigue, insomnia and impaired concentration. Travel fatigue usually disappears after a good rest and a night of sleep (Waterhouse et al., 2007).

After the flight, it is recommended to adapt the inner rhythm as fast as possible to the external rhythm. Adjusting the biological clock to the local rhythm is easier if the clock is already (partially) phase delayed or advanced, like discussed earlier. Nevertheless, there are some strategies to get rid of jet lag and its symptoms faster with the help of, amongst others, light also when no phase delay or advance has been induced. Since light is the most important time cue for circadian rhythms, it is the primary factor for determining the speed of readjustment to the new circadian clock after arrival (Bear, 2007; Sack, 2009). To adjust faster after an eastward flight, it is helpful to be exposed to bright light immediately after waking up. To adjust the internal time faster to the local time after a westward flight, it is better to be exposed to bright light at 'home' sleeping time.

Regarding taking melatonin, it is questionable whether it would be helpful not only when flying eastward, but also when going west. Since it helps falling asleep, it is most likely only helpful when flying east. That is when insomnia is the most common jet lag symptom and we have to sleep before our body's sleeping time, which is harder than going to sleep after our body's sleeping time, because then we are more tired. When going west, there should not be any problems with falling asleep, but with waking up early in the morning. In that case melatonin will be less helpful, since it mainly facilitates falling asleep and not necessarily maintaining sleep. Taking melatonin at bedtime after an eastward flight is recommended, in contrast to taking it after a westward flight at bedtime. The latter could inhibit phase resetting, while the first could be beneficial for phase resetting. Petrie, Conaglen, Thompson, and Chamberlain (1989) support melatonin as an aid for jet lag with a study where they compared two groups that crossed 8 time zones, one group eastward, the other westward. The people taking melatonin afterwards were significantly faster with realignment and had less jet lag symptoms than the ones who did not take melatonin. Also, melatonin as phase adjuster seems to work better with higher doses, up to 20 mg (Sack, 2009). Other circadian rhythm realignment tools like caffeine do only seem to be helpful to increase alertness. Meals at the appropriate times and social agenda seem to enhance circadian adaptation as well, as they work as 'Zeitgeber' or exogenous rhythms (Samuels, 2012).

With regard to timing of flying, Waterhouse et al. (2002) conducted a study where they observed a sports team during its flight from the United Kingdom to Australia. The whole journey would take about 24 hours. One of the independent variables was arrival time in Australia. One flight left in the morning (arriving in Australia in the afternoon, local time), group 1, and the other in the evening (arriving early in the morning at local time), group 2. The morning departure would go to sleep at night after being up for 30-35 hours and the evening departure after being up for 50-55 hours. Regarding this information, one would suggest that the morning group (1) would suffer less from fatigue than the other group (2). The results showed that the group that would arrive in the morning, group 2, slept significantly more during the flight. The group that arrived later in the day, group 1, had fewer problems with jet lag effects. Another finding was that the people on the evening flight, group 2, suffered more from fatigue in the noon and afternoon than the other group did. The phase disruption is less for the morning departure group 1. They lost less hours of sleep than the second group because the time period between the last and next full sleep is shorter. So arriving later on the day after an eastward flight is more beneficial for the traveler than arriving early(Waterhouse et al., 2002). It also seems to be beneficial to choose daytime flight as such that it minimizes sleep loss. Additionally to eventually take some melatonin or hypnotics to induce some sleep at night flights to minimize the fatigue and loss of sleep (Haimov & Arendt, 1999).

Summarized, the best way to avoid or minimize jet lag is to phase advance or delay the circadian rhythm as close as possible to the destination time rhythm a few days before the journey starts. Depending on direction and flight duration, the most beneficial sleep, departure and arrival times can be variable.

JET LAG AND FREQUENT TRAVELING

When flying frequently and crossing many time zones east and west, it can be very exhausting to adjust from one circadian rhythm to the other. How do shift workers, aircraft cabin crew, and other frequent flyers deal with this, especially since such travelers (or employees) suffer often or chronically from jet lag (Sack, 2009)?

In a study by Waterhouse et al. (2002), jet lag effects were measured in athletes after eastward flights from the United Kingdom to Australia. The results showed that the athletes who traveled the same journey before experienced the jet lag worse than the subjects that had not made the journey before. Also, the subjects that had traveled to Australia before showed more fatigue at noon and in the afternoon than the subjects for who this trip was the first time. This might have been due to the fact that they were more impressed and occupied by the new experiences and did not know what to expect and therefore probably paid less attention to the symptoms, as opposed to the subjects that had done the journey previously (Waterhouse et al., 2002).

Due to the few and limited studies or methods on how pilots and other frequent travelers deal with the regular jet lag troubling, we can only suggest how they recover or deal with the recurrent jet lags. The most convenient approach, especially for short duration trips, would be to maintain the same sleep schedule like at home. With this approach, the circadian rhythm would not change, which means that it does not have to realign and consequently no realignment symptoms (jet lag) would occur. If travelers do this, they sleep better and longer and have less jet lag effects. The only problem with this approach would be the social activities at the local destination, which they might not be able to attend because they are sleeping at home times. If the trips are of longer duration, it is important to adjust as fast as possible to the new circadian alignment, which can be done by earlier mentioned methods (Sack, 2009). A study done by Petrie, Dawson, Thompson, and Brook (1993) showed that taking melatonin may have benefits for cabin crew for a faster recovery from jet lag.

If the cause of jet lag is understood and when it can be counteracted, some health issues can be resolved in advance, as frequent jet travel and regularly being jet lagged has some health implications. Some of them are cognitive deficits, temporal lobe atrophy and menstrual cycle disturbances (Eastman & Burgess, 2009). Also, meals will be eaten at inappropriate circadian phase moments and repeated occurrence of this can cause weight gain which in turn can increase the risk of getting diabetes and cardiovascular problems. In short, frequent traveling is not beneficial for health and depending on the duration of the trip, it can be better to maintain the home sleep scheduled (Eastman & Burgess, 2009).

DISCUSSION

The primary aim of this review was to describe jet lag and its determinants and what can be done about it. The misalignment, the process of realignment and the symptoms after crossing time zones too fast for the biological clock to keep up, are collectively referred to as 'jet lag'. It turns out that many factors contribute to jet lag and its severity. As mentioned earlier, one of the contributing factors is flight direction. Flying eastward brings about more severe and persistent symptoms than flying westward (Auger & Morgenthaler, 2009; Haimov & Arendt, 1999; Kalat, 2010). Lemmer et al. (2002) show that athletes who flew eastward needed more time to adjust to the new rhythm than the athletes who flew westward. However, the eastward flight crossed two more time zones than the westward flight. Hence, all we can conclude from this study is that the crossing of more time zones brings about more persistent symptoms. Additional studies should investigate this effect with comparing east- and westward flights of equal time length. Perhaps return flights are suited for this kind of research. Both between-subject and within-subject effects can be explored this way.

Another factor which is said to influence the ability to cope with jet lag is age. However, there is disagreement about this. It is suggested that elderly people have more severe and longer lasting jet lag symptoms than younger people (Cooper, 2006; Waterhouse et al., 2002). Whether or not this is the case, still needs to be investigated. Studies that have confirmed these findings are simulations of phase shifting (Auger & Morgenthaler, 2009; Monk et al., 1993). The participants never crossed time zones and did not experience the social agenda after arrival because the study took place in an isolated and adjusted environment. Moreover, one study suggests that older people seem to be better in adjusting their circadian temperature to the new circadian rhythm than younger people (Monk et al., 1993). Besides these contradictive findings, there might be a problem in the definition of jet lag in the mentioned studies. The actual definition (symptoms of a misalignment of the circadian rhythm to the new local time) might be mistaken for general travel fatigue. Another limitation is that there are only studies done on phase advancing simulation and not on phase delaying. Future studies should take these limitations into account by using data of elderly flight passengers when 'naturally' crossing times zones instead of simulating time zone crossing. This is also more cost-efficient.

Another question in this review was whether it is possible to avoid or minimize jet lag symptoms. The literature only suggests ways to minimize symptoms and not to avoid them. The most efficient way to do so is to phase-advance or -delay the inner clock for respectively east- or westward crossing of time zones. The more the biological clock is adjusted prior to the journey, the easier it is to realign to 'the rest' of the rhythm. Even though these are the most effective methods, they have to be done with care. The delaying or advancing has to be done gradually; if the 'manual' phase shifting is done too fast, the inner circadian clock will not be able to keep up and jet lag symptoms will be experienced even before the actual flight (Eastman et al., 2005). However, even though phase shifting the circadian rhythm is more beneficial than only trying to minimize the symptoms after an abrupt time zone transition, it is not effortless. One has to make an effort to actually carry out the rhythm pre-adjustment. The largest sacrifice of advancing or delaying the sleeping schedule though, might be the missing out on social events and activities (Eastman et al., 2005).

To realign the inner and outer circadian rhythms after the flight, it is helpful to give the inner clock exogenous 'Zeitgebers' as realignment guide. These can be meals or social agenda for example. More important however is exposure or avoidance of bright light and taking melatonin at appropriate times. Although this can be troublesome if there is no access to bright light due to weather circumstances or an activity schedule. Also, the effect of light seems to vary with age, psychiatric status and changes in sleep homeostasis (Gaggioni et al., 2014).

Last but not least, the effect of frequent traveling on jet lag was explored. One would expect it causes habituation and consequently more ease to deal with, however, the opposite seems to be the case in the only study found on this issue. Athletes that traveled frequently suffered more from jet lag symptoms than athletes new to traveling (Waterhouse et al., 2002). This suggests that frequent time zone crossing rather brings awareness of jet lag symptoms instead of habituation or tolerance. However, if one travels often through time zones, it will be easier to learn how to adjust as fast as possible to the new circadian cycle. It should be clear that further research on the relation between jet lag and frequent traveling is necessary to elucidate the effects.

As known for now, jet lag severity is most dependent on the circumstances on the flight rather than personal differences, as there is limited evidence for the latter. Flight direction can make a difference, and so do flight duration and amount of time zones are crossed. Jet lag from flying eastward seems harder to overcome than after flying westward and it makes a big difference when one adjusts his or her circadian home rhythm to the rhythm of the destination. The current methods to minimize jet lag symptoms seem to work, although they are not without effort.

This literature research has thrown up many questions in need of further investigation. Now that we know that there are methods to minimize jet lag, it becomes interesting to think about the possibility to ever become resistant for circadian shifting. It is of special interest for shift workers, athletes and air craft crew, even more than knowing how to suffer as little as possible from jet lag. Hence, maybe this could be the next step in research about how to cope with jet lag, shift work and traveling through time zones. Furthermore, one could think about establishing the effects of personal differences such as the difference between 'night-owls' and 'morning-birds' in their relationship to jet lag. It is known that the two benefit from different strategies concerning phase-advancing and delaying, but specific studies are necessary to elucidate the exact relationship. Another future direction is age; many contradicting effects can be sorted out by studying the effect of time-zone crossing in higher age travelers instead of simulating in an unnatural environment. As a final suggestion for future work, the effects of light on cognitive functioning and the differences in effectiveness of light with regard to age, morning or evening person and psychiatric status should be explored in detail.

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