

doi 10.15171/ijtmgh.2019.09



Review Article

Open Access

Lagging Behind – The Emerging Influence of Jet Lag Symptoms on Road Safety



Shang Yuin Chai¹, Gerard Thomas Flaherty^{1,2*}

¹School of Medicine, National University of Ireland Galway, Galway, Ireland ²School of Medicine, International Medical University, Kuala Lumpur, Malaysia

Corresponding Author: Gerard Thomas Flaherty, MD, Professor, School of Medicine, National University of Ireland Galway, Galway, Ireland. Tel: +353-91495469, Fax: +353-91494540, Email: gerard.flaherty@nuigalway.ie

Received February 22, 2019; Accepted March 30, 2019; Online Published April 20, 2019

Abstract

Road traffic accidents are the leading cause of death in international travelers. With the growth of international travel, the number of visitors who rent a vehicle upon arrival at their destination by air or by sea is expected to increase. Jet lag is a well-recognized maladaptation to international travel across multiple time zones. Little is known about the possible influence of jet lag symptoms on the risk of road traffic collisions. Lack of awareness or failure to recognize the debilitating effects of jet lag and driving immediately after a long-haul flight put the driver at risk of a fatal road traffic accident. This article summarizes the available evidence and suggests reasonable approaches which may serve to minimize the risk of jet lag-induced driver fatigue leading to road injuries and deaths. The future research agenda should focus on routinely recording whether jet lag was a co-factor in road traffic accidents, analyzing the effectiveness of public awareness campaigns to highlight this neglected issue, and investigating the impact of jet lag on pedestrian road safety.

Keywords: Jet Lag, Trauma, Accidents, Traffic

Citation: Chai SY, Flaherty GT. Lagging behind - the emerging influence of jet lag symptoms on road safety. Int J Travel Med Glob Health. 2019;7(2):39-44. doi:10.15171/ijtmgh.2019.09.

Introduction

With the growth in international travel, the number of visitors who rent a vehicle upon arrival at their destination by air or by sea is expected to rise. According to the car rental industry in Ireland, over 40% of all US tourists and close to half of visitors from all countries rented a car in 2017 (https:// www.euromonitor.com/car-rental-in-ireland/report). After a long-haul flight, especially a transmeridian flight that crosses multiple time zones, most people experience a state of fatigue, mental disturbance, and an unpleasant feeling of dysphoria termed jet lag.¹ Jet lag syndrome may pose a significant threat to road safety when international travelers, be they inbound or outbound, choose to drive on the road with jet lag symptoms.

This subject has been neglected in the traffic medicine scientific literature. This review article will explore the phenomenon of jet lag and its relationship with road safety. Relevant material was sourced by comprehensively searching the PubMed database using combinations of the keywords "travel", "road safety", "jet lag", and "accident". A manual search of the reference lists of articles was also conducted, and the grey literature provided an additional source of important background material.

Jet Lag Syndrome

According to the 5th Diagnostic and Statistical Manual of Mental Disorders (DSM-V), jet lag is classified as a circadian rhythm sleep disorder which results in disturbance of the sleep-wake cycle.² The circadian rhythm is a physiological process that is coordinated internally with changes in body hormone secretion and temperature over a period of 24 hours.³ This occurs in synchrony with environmental time cues also known as zeitgebers, the light-dark cycle and the secretion of melatonin being the strongest time cue influencing the circadian rhythm.⁴ Hence, rapid travel across time zones leads to misalignment between the internal biological clock and environmental zeitgebers.

Symptoms of jet lag include fatigue, disturbed sleep and wakefulness, impaired alertness, irritability, and sometimes changes in bowel habits and urinary symptoms. A derangement of normal circadian rhythm alters the sleep-wake pattern. Laboratory studies show that this so-called displaced sleep is strongly associated with impairment of mental performance.⁵ Research into aircrew performance during long-haul flights and flights across multiple time zones has revealed decrements in psychomotor, vigilance, and cognitive performance based on neuropsychological tests.5

Copyright © 2019 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (http:// creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Effect of Jet Lag on Driving

Driving a vehicle in a normal traffic environment requires a high cognitive load associated with full attention, sound judgment, and a prompt reaction speed.⁵ With the limited number of studies published, there is a lack of evidence asserting a direct association between jet lag and road traffic accidents. Jet lag-induced fatigue results in sleep deprivation in drivers, which leads to diminished concentration, deterioration in alertness, and impaired decision-making.⁶ Sleepiness while driving is a significant contributor to road traffic collisions.⁷ Lack of awareness or failure to recognize the debilitating effects of jet lag and driving immediately after a long-haul flight put drivers at risk of a fatal road traffic accident.

Risk Factors for Jet Lag

Circadian misalignment from jet lag crossing several time zones usually dissipates in a few days.8 The effects of jet lag differ between individuals based on their susceptibility, and considerable variation exists in the rate of physiological adaptation to a new local time zone.3,4,9 Jet lag syndrome is more pronounced when the traveler does not receive adequate sleep, where sleep is of short duration, where there is an underlying sleep disorder, or where sleep is disturbed by other passengers or air crew during the flight.9 For unknown reasons, the rate of adaptation to local time cues seems to decrease as people get older.¹⁰ Different ethnic groups also display different recovery times from jet lag. One study found that African-Americans are more likely to suffer longer periods of jet lag regardless of the direction of the flight when compared to European-Americans.¹¹ Hence, the management of jet lag may be more important among African-American travelers. European-Americans are found to have a larger phase delay which permits them to have adequate sleep and prevents early awakenings usually seen after westward flights.11

Light is one of the strongest zeitgebers and has a profound influence on the human circadian rhythm. Researchers speculate that this may have been a process of natural selection occurring over thousands of years whereby Europeans living in northern latitudes had to adapt to photoperiods, or durations of sunlight, that change with seasons.¹² Furthermore, it is reported that salivary cortisol levels increase significantly when travelers cross more than one time zone and to a greater extent with eastward travel.13,14 This study hypothesized that a short-term shift in the diurnal cortisol pattern is adaptive rather than harmful; however, further research is required to better understand this beneficial property as an "awakening" hormonal response. There are also possible long-term consequences of physiological, psychological, and cognitive deficits in chronic shifts of diurnal patterns associated with frequent flying or routine travel.¹⁵

Influence of Flight Direction on Jet Lag

The direction of the flight also has an impact on the severity of jet lag. Many studies have reported that flying in an eastward direction exerts a more pronounced jet-lag effect than flights in a westerly direction.^{8,9,13,16} After an eastward flight, travelers

usually experience difficulties in falling asleep at night and sleepiness in the morning. The effect of sleepiness after an eastward flight is milder, but adjustment takes a longer period to re-entrain normal circadian rhythms.^{5,8} One possible explanation for this phenomenon might be that travelers are often exposed to light on arrival at their destination that induces a phase shift, which deranges the normal circadian rhythm during their circadian low, the period when the body is programmed to sleep.16 In addition, many travelers often adjust and phase shift in the wrong direction. To apply it to a real-life jet lag situation, with 8 hours advance phase shifts of zeitgebers, which is similar to flying eastward across 8 time zones, travelers adjust by delaying phase shifts by 16 hours (adjustment in a westward direction) instead of advancing 8 hours. One study found that ethnic groups with larger phase delays (such as European-Americans) are more likely to adopt this antidromic re-entrainment.¹⁷

Moreover, westward flights crossing more than 5 time zones result in evening sleepiness and early morning awakening in travelers. Westward travel is associated with a shorter period of recovery and causes less disruption than eastward travel as it is easier to lengthen our natural circadian rhythm.¹⁸ However, it is also important to note the time of the day on arrival. Some would argue that late afternoon and evening arrival times are associated with the highest incidence of road traffic accidents, stemming from the fact that light is starting to diminish during these hours.¹⁹ For westward travelers arriving at evening time, driving in poor lighting conditions is considered less favorable for road users, especially immediately after a long-haul flight when jet lag symptoms are starting to appear. The summation effects of jet-lag induced fatigue, a delayed phase shift in the circadian rhythm causing sleepiness, and poor lighting conditions on roads are contributing factors that are implicated in the increased risk of road traffic injuries and fatalities at night.²⁰

Jet lag-induced fatigue is more severe following a long-haul flight that crosses multiple time zones.⁸ A survey of 739 pilots reported that fatigue during a long-haul flight was mainly due to night-time flights and jet lag that results in sleep deprivation.²¹ Self-reported manifestations of fatigue in 60% of the long-haul flight pilots included impairment of attention and alertness and a lack of concentration. A questionnairebased study in the United States found that airline passengers on a long-haul flight were more likely to consume alcoholic drinks on board. The authors concluded that alcohol was less likely to worsen jet lag.²² Further studies are still required to gain a deeper understanding of the disruption of the circadian clock and the length of recovery from jet lag in order to minimize the potential threat it poses to road users.

Role of Melatonin in the Management of Jet Lag

There are several ways to minimize the effects of jet lag, either by lifestyle measures or pharmacological interventions.⁸ The primary symptom of jet lag among travelers is sleep disturbance.²³ Sedative-hypnotics or stimulants may be useful in counteracting this symptom. The secretion of the neurohormone melatonin is a crucial time cue in mediating the rhythmic sleep-wake pattern and regulating the circadian

rhythm.24 Under the influence of the light-dark cycle, it moderates the secretion by the pineal gland, where darkness switches on melatonin secretion while light inhibits its secretion.²¹ Thus, the signaling of melatonin in the night increases the natural tendency to sleep.25 Clinical studies have provided strong evidence that melatonin supplements reduce the severity of jet lag and improve the quality of sleep in both eastward and westward travel when compared to placebo and have minimal side effects.²⁶ Given the complexity of synchronizing the properties of melatonin with the sleepwake cycle, precise timing and careful administration of melatonin together with light exposure should be exploited for optimal effects to induce proper phase shifting.²⁷ One randomized controlled trial found that taking melatonin after arrival reduced the severity of jet lag when compared to its administration before and after flights.8 Melatonin is not currently licensed in many countries for the prevention or relief of jet lag symptoms.

Sedative-Hypnotics and Jet Lag

Sleep can also be promoted by the administration of hypnotics.²⁸ Administration of benzodiazepine hypnotics and zopiclone before bedtime in the first few nights after a flight has been shown to improve sleep quality.⁸ However, the residual hangover effects the following morning produces a significant impairment in driving performance. Non-benzodiazepine hypnotics (e.g., zolpidem) have no significant hangover effect the next morning.²⁹ However, most hypnotics do not re-entrain the underlying desynchrony and are usually only recommended in situations when adaptation is undesirable and for short stopovers.⁹ For example, hypnotics such as temazepam can be useful in air crew to facilitate sleep during the period between landing and flying out without significantly impairing psychomotor performance.³⁰

Use of Stimulants in Jet Lag

Other possible pharmaceutical approaches include the use of stimulants that increase driver alertness. The drugs modafinil and armodafinil have shown promising effectiveness in treating daytime sleepiness and shift-work disorder. Both drugs have been approved by the US Food and Drug Administration (FDA) and were initially developed to treat excessive daytime sleepiness disorder, but have yet to be approved for use in treating jet lag to maintain alertness.9 Caffeine can also promote alertness during desired times of wakefulness and improve cognitive performance in jet-lagged subjects.31 Thus, caffeine may be of great importance in maintaining daytime alertness and improving attention and orientation while driving in a new time zone. Just like sleeppromoting melatonin, correctly timed dose administration of caffeine needs to be considered as it may result in disturbed nocturnal sleep.32 It is important to stress that all pharmacological interventions do not re-entrain the circadian rhythm immediately or alleviate underlying jet lag syndrome instantly, but work by hastening the recovery period.9

Light Exposure in Jet-Lagged Travelers

Another aspect of managing jet lag is lifestyle and

environmental adaptation. Light exposure, either through natural sunlight or artificial bright light, has the effect of promoting alertness as well as mediating a phase-shifting effect on the circadian rhythm.³³ Light avoidance at critical times is crucial in adjusting to new time zones. Theoretically, exposure to light during the start of the "biological evening", coinciding with the rise in endogenous melatonin, delays the circadian rhythm, and during late "biological dusk" (a fall in endogenous melatonin) it advances the circadian rhythm.³⁴ Seeking or avoiding light at the correct time is crucial in phaseshifting, together with the administration of melatonin that can act synergistically with respect to phase-shifting.³⁵ After a westward flight, it is worth staying awake during the day and seeking light in the early evening to delay the synchronization of the circadian rhythm with the new time zone. Conversely, exposure to sunlight early in the day and being outdoors as much as possible during the day are recommended after an eastward flight to advance the circadian rhythm.³⁶

Recently, much attention has focused on food entrainment and its putative role in promoting peripheral resynchronization. Although further research is required to support this finding, it is recommended to eat at the conventional time in the local time zone of the destination.⁹ One interesting mouse model experiment conducted in Japan concluded that mice cope better with jet lag when they are "pre-sensitized" to it.³⁷ The researchers believed that this may also apply to humans, for example, waking up four hours early on the day before a longdistance eastbound trip.³⁷

Jet Lag as a Risk Factor for Road Traffic Collisions

Traffic medicine, which focuses on the medical fitness to drive,³⁸ is still in its infancy as a medical discipline, but it is already proving to be a fertile domain for original research.³⁹ Jet lag and its effect on motorist behavior and performance is just one area of collaborative research potential between travel medicine and traffic medicine. Others include prioritization of road safety in pre-travel consultations,⁴⁰ clearance to drive overseas in travelers with pre-existing medical conditions,⁴¹ responsible traveler driving behavior overseas,⁴² and analysis of road traffic accidents as a cause of death in international travelers.⁴³

Understanding the role that jet lag plays as a risk factor in road traffic accidents is a critical first step in minimizing injury and fatal collisions. If going on vacation and renting a vehicle is part of the traveler's itinerary, it is important to take precautions and ensure that the journey is well-planned, including being aware of the incidence of road traffic accidents in the country being visited. It is not recommended to rent a vehicle upon reaching the destination and drive away from the airport immediately if the flight arrives at night or after a long-haul flight crossing more than five time zones. A safer option is to use a safe and economic method of public transportation such as the express rail link from airport to city, hotel shuttle bus, or taxi. Moreover, navigating with unfamiliar signage in a foreign country, driving with the steering wheel on the other side of the car, or a lack of familiarity with local driving conditions, customs, and traffic laws all increase the odds of being involved in a road traffic accident. Arranging

a pick-up from the airport with a family member or friend is also advisable and a safer way to get home or to a hotel. It is essential for drivers to recognize that driving while jet lagged is never safe. If driving away from an airport after an overnight or long-haul flight is unavoidable, the driver should be advised to stop and nap for a few minutes, or even to get out of the car to take some fresh air.

Table 1 summarizes recommendations based on the authors' clinical experience in travel medicine for the promotion of road safety behavior in international travelers who may be subject to jet lag.

Future Developments in Jet Lag Road Safety

There is a pressing need for an awareness program to educate the public about the potential consequences of jet lag in order to reduce jet lag-induced fatigue-related road traffic accidents. The contribution of jet lag-induced fatigue in road traffic accidents is under-appreciated when compared to other causes of road traffic accidents such as speed driving or driving while intoxicated with alcohol.⁴⁴ The complexity of collecting largely self-reported data, which increases the risk of recall bias and misclassification, limits the evidence of a robust relationship between jet lag and road traffic accidents.45 Mobile health technology presents multiple opportunities to enhance travel health and security, including its use in accelerating acclimatization to a new time zone.46 Developments in technology for detecting and possibly measuring jet-lag induced fatigue using a real-time tracking device⁴⁷ or AdaBoost Classifier with EEG Signals⁴⁸ may have a future role in promoting traffic safety in the context of jet-lagged drivers. Road safety should be considered in the context of multiple traumatic and non-communicable disease health risks faced by international travelers, a neglected area of travel medicine research.49,50

Conclusion

Theoretically, and based on the available research data, jet lag should be regarded as an important factor in the causation of motor vehicle trauma in arriving international passengers. The future research agenda should focus on routinely recording whether jet lag was a co-factor in road traffic accidents, analyzing the effectiveness of public awareness campaigns to highlight this neglected issue, and investigating the impact of jet lag on pedestrian road safety. Far from lagging behind, the

Review Highlights

What Is Already Known?

While jet lag is frequently discussed as part of the pretravel consultation, the effect of jet lag on the risk of traffic injuries and fatalities in drivers has not been well studied.

What This Study Adds?

This article discusses the jet lag in the context of international travel and it explores the effects of jet lag and sleep deprivation on driver behavior abroad. A series of practical recommendations are presented which may serve to reduce the burden of jet lag-induced road traffic incidents. Recommendations for further research are proposed.

travel medicine community is in an ideal position to lead the way in jet lag-related road safety research.

Authors' Contributions

Both Authors contributed equally to this study.

Conflict of Interest Disclosures

None declared.

Ethical Approval

Not applicable.

Funding/Support

None received.

References

- Waterhouse J, Reilly T, Atkinson G. Jet-lag. Lancet. 1997;350(9091):1611-1616. doi:10.1016/s0140-6736(97)07569-7.
- Thorpy MJ. Classification of sleep disorders. Neurotherapeutics. 2012;9(4):687-701. doi:10.1007/s13311-012-0145-6.
- Ker K, Edwards PJ, Roberts I, Blackhall K, Felix LM. Interventions for preventing injuries caused by impaired alertness in individuals with jet lag and shift work disorder. Cochrane Database Syst Rev. 2009(2). doi:10.1002/14651858.cd007741.
- 4. Waterhouse J, Reilly T, Atkinson G, Edwards B. Jet lag: trends and coping strategies. Lancet. 2007;369(9567):1117-1129. doi:10.1016/s0140-6736(07)60529-7.
- 5. Akerstedt T. Altered sleep/wake patterns and mental performance.

Table 1. Recommendations for the Prevention of Jet Lag-Related Road Traffic Accidents

Road Safety Issue	Recommendation
Itinerary planning	Ensure a well-planned travel itinerary.
Road safety statistics	Familiarize oneself with national road traffic accident data.
Vehicle hire	Avoid hiring a vehicle from the airport if arriving jet-lagged, especially for eastward flights.
Direction of travel	Time light exposure to accelerate adjustment to local time zone for eastward travel.
Alternative transportation	Arrange private pick-up or public transportation from airport if arriving on a long-haul flight.
Insurance	All travelers should have comprehensive travel insurance and the required international driver license.
Alcohol consumption	Alcohol should be avoided if planning to drive from the airport to a hotel or home.
Local traffic laws	Travelers should respect and obey all local traffic laws.

Physiol Behav. 2007;90(2-3):209-218. doi:10.1016/j. physbeh.2006.09.007.

- 6. Killgore WD, Balkin TJ, Wesensten NJ. Impaired decision making following 49 h of sleep deprivation. J Sleep Res. 2006;15(1):7-13. doi:10.1111/j.1365-2869.2006.00487.x.
- Herman J, Kafoa B, Wainiqolo I, et al. Driver sleepiness and risk of motor vehicle crash injuries: a population-based case control study in Fiji (TRIP 12). Injury. 2014;45(3):586-591. doi:10.1016/j. injury.2013.06.007.
- 8. Herxheimer A. Jet lag. BMJ Clin Evid. 2014;2014.
- Arendt J. Approaches to the pharmacological management of jet lag. Drugs. 2018;78(14):1419-1431. doi:10.1007/s40265-018-0973-8.
- 10. Becker T, Penzel T, Fietze I. First jet lag symptoms after travelling across multiple time zones. Biol Rhythm Res. 2015;46(3):361-370. doi:10.1080/09291016.2015.1015230.
- 11. Eastman Cl, Tomaka VA, Crowley SJ. Circadian rhythms of European and African-Americans after a large delay of sleep as in jet lag and night work. Sci Rep. 2016;6:36716. doi:10.1038/ srep36716.
- Pittendrigh CS, Daan S. A functional analysis of circadian pacemakers in nocturnal rodents. IV. Entrainment: pacemaker as clock. J Comp Physiol. 1976;106(3):291-331. doi:10.1007/ bf01417856.
- Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr Rev. 2000;21(1):55-89. doi:10.1210/edrv.21.1.0389.
- Doane LD, Kremen WS, Eaves LJ, et al. Associations between jet lag and cortisol diurnal rhythms after domestic travel. Health Psychol. 2010;29(2):117-123. doi:10.1037/a0017865.
- Cho K, Ennaceur A, Cole JC, Suh CK. Chronic jet lag produces cognitive deficits. J Neurosci. 2000;20(6):Rc66. doi:10.1523/ JNEUROSCI.20-06-j0005.2000.
- 16. Wegmann HM, Klein KE, Conrad B, Esser P. A model for prediction of resynchronization after time-zone flights. Aviat Space Environ Med. 1983;54(6):524-527.
- Eastman CI, Suh C, Tomaka VA, Crowley SJ. Circadian rhythm phase shifts and endogenous free-running circadian period differ between African-Americans and European-Americans. Sci Rep. 2015;5:8381. doi:10.1038/srep08381.
- Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag. In: The Cochrane Library, Issues 12. Chichester, UK: John Wiley & Sons Ltd; 2013.
- Broughton J, Stone M. A new assessment of the likely effects on road traffic accidents of adopting SDST. Transport Research Laboratory; 1998.
- 20. Carey RN, Sarma KM. Impact of daylight saving time on road traffic collision risk: a systematic review. BMJ Open. 2017;7(6):e014319. doi:10.1136/bmjopen-2016-014319.
- 21. Bourgeois-Bougrine S, Carbon P, Gounelle C, Mollard R, Coblentz A. Perceived fatigue for short- and long-haul flights: a survey of 739 airline pilots. Aviat Space Environ Med. 2003;74(10):1072-1077.
- 22. Girasek DC, Olsen CH. Airline passengers' alcohol use and its safety implications. J Travel Med. 2009;16(5):311-316. doi:10.1111/j.1708-8305.2009.00339.x.
- 23. Sack RL. The pathophysiology of jet lag. Travel Med Infect Dis. 2009;7(2):102-110. doi:10.1016/j.tmaid.2009.01.006.
- Zisapel N. New perspectives on the role of melatonin in human sleep, circadian rhythms and their regulation. Br J Pharmacol. 2018;175(16):3190-3199. doi:10.1111/bph.14116.
- 25. Cramer H, Rudolph J, Consbruch U, Kendel K. On the effects of melatonin on sleep and behavior in man. Adv Biochem Psychopharmacol. 1974;11:187-191.

- Arendt J, Skene DJ, Middleton B, Lockley SW, Deacon S. Efficacy of melatonin treatment in jet lag, shift work, and blindness. J Biol Rhythms. 1997;12(6):604-617. doi:10.1177/0748730497012006 16.
- Arendt J. Managing jet lag: Some of the problems and possible new solutions. Sleep Med Rev. 2009;13(4):249-256. doi:10.1016/j. smrv.2008.07.011.
- Coste O, Lagarde D. Clinical management of jet lag: what can be proposed when performance is critical? Travel Med Infect Dis. 2009;7(2):82-87. doi:10.1016/j.tmaid.2008.08.004.
- 29. Pandi-Perumal SR, Verster JC, Kayumov L, et al. Sleep disorders, sleepiness and traffic safety: a public health menace. Braz J Med Biol Res. 2006;39(7):863-871. doi:10.1590/s0100-879x2006000700003.
- Reilly T, Atkinson G, Budgett R. Effect of low-dose temazepam on physiological variables and performance tests following a westerly flight across five time zones. Int J Sports Med. 2001;22(3):166-174. doi:10.1055/s-2001-16379.
- 31. Ker K, Edwards PJ, Felix LM, Blackhall K, Roberts I. Caffeine for the prevention of injuries and errors in shift workers. Cochrane Database Syst Rev. 2010(5):Cd008508. doi:10.1002/14651858. cd008508.
- 32. Morgenthaler TI, Lee-Chiong T, Alessi C, et al. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An American Academy of Sleep Medicine report. Sleep. 2007;30(11):1445-1459. doi:10.1093/sleep/30.11.1445.
- Czeisler CA, Johnson MP, Duffy JF, Brown EN, Ronda JM, Kronauer RE. Exposure to bright light and darkness to treat physiologic maladaptation to night work. N Engl J Med. 1990;322(18):1253-1259. doi:10.1056/nejm199005033221801.
- Khalsa SB, Jewett ME, Cajochen C, Czeisler CA. A phase response curve to single bright light pulses in human subjects. J Physiol. 2003;549(Pt 3):945-952. doi:10.1113/jphysiol.2003.040477.
- Paul MA, Gray GW, Lieberman HR, et al. Phase advance with separate and combined melatonin and light treatment. Psychopharmacology (Berl). 2011;214(2):515-523. doi:10.1007/ s00213-010-2059-5.
- Freedman DO, Chen LH, Kozarsky PE. Medical considerations before international travel. N Engl J Med. 2016;375(3):247-260. doi:10.1056/NEJMra1508815.
- 37. Kori H, Yamaguchi Y, Okamura H. Accelerating recovery from jet lag: prediction from a multi-oscillator model and its experimental confirmation in model animals. Sci Rep. 2017;7:46702. doi:10.1038/srep46702.
- Kahvedzic A, McFadden R, Cummins G, Carr D, O'Neill D. Impact of new guidelines and educational program on awareness of medical fitness to drive among general practitioners in Ireland. Traffic Inj Prev. 2015;16(6):593-598. doi:10.1080/15389588.201 4.979408.
- Groneberg-Kloft B, Klingelhoefer D, Zitnik SE, Scutaru C. Traffic medicine-related research: a scientometric analysis. BMC Public Health. 2013;13:541. doi:10.1186/1471-2458-13-541.
- 40. Flaherty GT, Chen B, Avalos G. Individual traveller health priorities and the pre-travel health consultation. J Travel Med. 2017;24(6). doi:10.1093/jtm/tax059.
- 41. Han CT, Flaherty G. Profile of travelers with preexisting medical conditions attending a specialist travel medicine clinic in Ireland. J Travel Med. 2015;22(5):312-317. doi:10.1111/jtm.12221.
- Lim BCW, Flaherty GT. Leaving light footprints the importance of promoting responsible international travel. Int J Travel Med Glob Health. 2018;6(3):88-91. doi:10.15171/ijtmgh.2018.18.
- Darrat M, Flaherty GT. Deaths of Irish civilians abroad: analysis of national mortality data, 2016-2018. Int J Travel Med Glob Health. 2018;6(4):149-153. doi:10.15171/ijtmgh.2018.27.
- 44. Dawson D, Reynolds AC, Van Dongen HPA, Thomas MJW.

Determining the likelihood that fatigue was present in a road accident: A theoretical review and suggested accident taxonomy. Sleep Med Rev. 2018;42:202-210. doi:10.1016/j. smrv.2018.08.006.

- Fung KY, Howe GR. Methodological issues in case-control studies. III--The effect of joint misclassification of risk factors and confounding factors upon estimation and power. Int J Epidemiol. 1984;13(3):366-370. doi:10.1093/ije/13.3.366.
- 46. Flaherty GT. Research on the move: the potential applications of mobile health technology in travel medicine. J Travel Med. 2016;23(6). doi:10.1093/jtm/taw061.
- 47. Xu J, Min J, Hu J. Real-time eye tracking for the assessment of driver

fatigue. Healthc Technol Lett. 2018;5(2):54-58. doi:10.1049/ htl.2017.0020.

- 48. Hu J. Automated Detection of Driver Fatigue Based on AdaBoost Classifier with EEG Signals. Front Comput Neurosci. 2017;11:72. doi:10.3389/fncom.2017.00072.
- 49. Long IJ, Flaherty GT. Traumatic travels a review of accidental death and injury in international travellers. Int J Travel Med Glob Health. 2018;6(2):48-53. doi:10.15171/ijtmgh.2018.10.
- Sanford CA, Flaherty GT. The significance of non-communicable threats to travellers: time for a sea-change? J Travel Med. 2018;26(1). doi:10.1093/jtm/tay103.