Current Psychiatry Reports (2019) 21: 127
https://doi.org/10.1007/s11920-019-1109-x

MILITARY MENTAL HEALTH (E MEYER II, SECTION EDITOR)

Impact of Smoking and Smoking Cessation Medications in Aviators

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Published online: 20 November 2019

Abstract

Purpose of Review To (1) compare the effects of cigarette smoking, nicotine withdrawal, and smoking cessation medications in US civilian and military aviators and (2) review the regulations in place regarding the use of smoking cessation medications for US aviators.

Recent Findings Cigarette smoking and associated cessation attempts are associated with multiple hazards in flight to aviators including effects from nicotine intoxication, nicotine withdrawal, carbon monoxide intoxication, and side effects related to smoking cessation medications. Current civilian and military regulations place significant restrictions on the use of smoking cessation medications to aviators; however, recent research suggests that the hazards associated with these medications might be lower than the risk-associated unassisted nicotine withdrawal.

Summary An evidence-based approach to smoking cessation may require changing restrictions against smoking cessation medication use in US civilian and military aviators. Use and cessation of smokeless tobacco and e-cigarettes require additional attention and research in this population.

Keywords Smoking cessation · Nicotine · Aviation · Bupropion · Varenicline

Introduction

Cigarette smoking is the leading cause of preventable death in the USA, responsible for approximately one in five deaths annually [1•]. Compared with non-smokers, smokers overall health is worse; they are sick more often, and they miss more time from work [1•]. While the percentage of active duty US Army soldiers who smoke cigarettes is lower than the civilian population when matched to age and gender, the rate remains prevalent at 14% of the total active duty population [2]. In 2015, more than two-thirds of US smokers reported wanting to quit completely, and 55.4% of all adult smokers had stopped smoking for more than 1 day because they were trying to quit [3]. Likewise, in the US Army, the rates of cigarette smoking have fallen nearly 7.0% from 2013 to 2017, even while the use of smokeless tobacco products has remained relatively flat [2]. Nevertheless, the harmful effects of smoking continue to be of particular concern to the military aviation community where optimum physiological functioning is critical in order to simultaneously cope with the potentially harmful effects of altitude, occupational toxins, environmental hazards, mission requirements, and enemy activity.

This paper reviews the potentially hazardous effects of cigarette smoking, unassisted nicotine withdrawal, and smoking cessation treatments among a broad spectrum of aviators. Furthermore, "aviators" herein refers to those personnel such as pilots and crewmembers who actually fly in aircraft. Other ground-based aviation personnel such as air traffic controllers and unmanned aerial system operators will not be discussed, though are often regulated by the same policies as the aviators to be discussed below.

This article is part of the Topical Collection on *Military Mental Health*

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Effects of Smoking in Aviation

The effects of smoking in aviation can be divided into nicotine's effects on human performance efficiency and hazards associated with carbon monoxide exposure. Nicotine is a potent psychoactive and cardiovascular medication that imparts both performance enhancement and degradation based on its presence or absence. As a cardiovascular stimulant, nicotine induces sympathetic neural stimulation increasing both blood pressure and heart rate [4, 5]. While this effect chronically is detrimental to cardiovascular health, acutely this increase in both blood pressure and heart rate is protective to sustaining G-forces in the aviation environment [6].

In the central nervous system, nicotine is a ganglionic and central nervous system stimulant that has been shown to improve information processing and enhance sensorimotor performance that are both beneficial in performing aviation duties [7, 8•]. Munmenthaler and colleagues demonstrated in a crossover double-blinded placebo-controlled study that pilots using nicotine increased cognition and coordination while performing critical tasks in a flight simulator [9–11]. However, nicotine's stimulating effects need to be avoided before bedtime because it can disrupt a pilot's ability to obtain restorative sleep increasing fatigue and the chance for an inflight error [12]. Moreover, although nicotine is commonly used by pilots for its stimulating effects, it is not an approved nor recommended countermeasure to combat fatigue in either the military or civilian aviation community [12].

In the absence of nicotine, over half of habituated users will demonstrate clinically significant withdrawal symptoms and distress [13]. Upon abstaining, users typically demonstrated symptoms of withdrawal within as a little as an hour following the last cigarette with most exhibiting symptoms within 12 to 24 h [13–15]. These symptoms usually peaked within the first week and lasted between 2 to 4 weeks [13–15]. Typical withdrawal symptoms for nicotine include anger, anxiety, depression, difficulty concentrating, impatience, insomnia, irritability, and restlessness [13–15]. These symptoms effect aircrew efficiency and pose a real risk to safe flight operations. Individual performance is degraded by psychomotor agitation caused by these symptoms leading to loss of sustained vigilance and task management, resulting in increased error rate during flight [15]. Moreover, the symptoms of anger, irritability, and impatience can negatively affect other aircrew members leading to a breakdown in crew coordination, which is paramount to safe flight operations. Thus, while nicotine is a stimulant and can lead to increased performance, its absence for even short periods of time can lead to significant degradation in crew and individual performance while flying.

The other hazard from smoking in aviation is carbon monoxide (CO) poisoning, which decreases resistance to hypoxia at altitude and degrades visual performance. Pilot impairment due to CO is a well-known hazard to safe flight operations, and required annual training for all Army aircrews to mitigate its effects [16•]. Smokers have a baseline level of carboxyhemoglobin of 4 to 5%, but can be upwards of 10% in heavy smokers [16•, 17]. Carbon monoxide causes both hypemic hypoxia and histotoxic hypoxia, through its high affinity binding to hemoglobin and its competitive inhibition of cytochrome c oxidase at the tissue level, respectively [6]. While the effects of hypoxia are not present below 10,000 ft mean sea level (ft MSL) due to sufficient cardiopulmonary compensatory mechanisms, these effects from CO cause the oxyhemoglobin curve to shift left leading to signs and symptoms of hypoxia at lower altitudes [6]. Work by Pitts and Pace demonstrated that a carboxyhemoglobin (COHb) level of 4% was equivalent to being at an altitude of 1500 ft MSL; thus, for the average and heavy smoker, symptoms of hypoxia would develop at 8500 ft MSL and 6250 ft MSL, respectively [18•]. Thus, smoking aviators must be aware of their increased susceptibility to hypoxia at lower altitudes because if not, they will be more likely to succumb to hypoxia's insidious effects leading to error in performing flight duties.

Vision is the most sensitive sensory organ to hypoxia and exhibits impairment at all altitudes [6]. Degradation of visual performance follows an out-to-in pattern with peripheral vision being affected first, followed by progressive degradation until central vision is affected as hypoxia worsens. Peripheral vision demonstrates a 5% decrement in night vision at 3000 ft MSL, which degrades to 50% by the time it is required by regulations to use onboard oxygen systems to combat hypoxia [6, 16•]. With increasing altitude, the eyes' ability to accommodate and converge degrades due to incoordination of extraocular muscles leading to blurred vision, which, in combination with aircraft vibration, makes carrying out near visual tasks, such as reading instruments, nearly impossible [6, 16•]. At significant altitudes (> 18,000 ft MSL), the visual system's reaction time and response to stimuli are so severely degraded that heterophorias cannot be compensated for, and diplopia develops [6]. Interestingly, vision is highly sensitive to carbon monoxide poisoning with levels of as little as 5% creating effects similar to flying at 9800 ft MSL, indicating that smokers are more likely to exhibit more severe vision degradation as they rise in altitude than non-smokers [6, 16•]. Moreover, smokers demonstrate a 15–18% degradation of night vision, decreased contrast sensitivity, and longer dark adaptation than non-smokers at sea level as a result of their baseline carbon monoxide levels [6, 19]. To complicate matters, carbon monoxide is the most common gaseous poison in the aviation environment due to incomplete combustion of aviation fuel [16•]. While carbon monoxide is ventilated away from the aircraft during flight, the exposure increases when the aircraft is in contact or close contact with the ground that occurs during run up, taxiing, or hovering. The carbon monoxide exposure is increased during cold weather in which exhaust heaters are used to heat the cabin in flight, or crew members while on the ground stand a safe distance from exhausts, such as the Auxiliary Power Unit (APU), to keep warm. All these exposures may add to smokers' baseline level of carbon monoxide, making them more susceptible to visual degradation and hypoxia.

Effects of Smoking Cessation Treatments in Aviation

Medical care among aviators is highly regulated, with specialized aeromedical examiners (or "flight surgeons" in the US military) continually assessing aviators' fitness for flight duties. Due to the unique physiological demands of sustained flight duties, even seemingly minor illness or over the counter medications could have life-threatening consequences. So while smoking has clear potential for harm in this population as above, smoking cessation can also be associated with increased risk. In fact, while there is admittedly a marked paucity of data specific to aviators, a review of smoking cessation medications from the Israeli Air Force Aeromedical Center went as far as to recommend banning all systemic smoking cessation medications in aviators while flying, with the exception of nicotine replacement therapies (NRTs) [20]. Yet even among NRTs, there are unique flight concerns with some formulations such as the theoretical potential for gum and lozenges to interfere with clear communications or become a choking hazard in flight.

Table 1 compares the current smoking cessation policies set by the FAA, US Air Force, US Army, and US Navy [21–24]. In general, nicotine replacement therapy (NRT) is allowed for smoking cessation, although often with at least a 48–72-h period of restriction from flying duty (or "grounding") [21–24]. Current Army regulations allow for use in flight following a 2-week grounding period [23], whereas Navy, Air Force, and the FAA do not allow use while on flight duty [21, 22, 24]. No US civilian or military service has a regulation allowing varenicline use while on flight duty, although it is worth noting that the Army's regulation has not been updated since 2002 and therefore does not specifically mention this medication at all [21–24].

In a recent exploration of side effects of these three FDA-approved smoking cessation medications, Anthelli et al. published the landmark "EAGLES" study comparing the nicotine replacement patch, bupropion, and varenicline among 8144 participants both with and without history of psychiatric illness [25••]. Among the non-psychiatric cohort most relevant to the aviation community, continuous abstinence rates at weeks 9–24 were found to be higher with varenicline (odds ratio (OR) = 2.99), bupropion (OR = 2.00), and nicotine patch (OR = 1.96) compared with placebo; and varenicline further outperformed both nicotine (OR = 1.62) and bupropion (OR = 1.74) as well. Due to concerns of neuropsychiatric side effects including suicidality with varenicline and bupropion treatment leading to a black box warning from the Food and Drug Administration (FDA) on these medications, the EAGLES study further looked in depth at several potential neuropsychiatric side effects and surprisingly found a lower rate of neuropsychiatric side effects (1.3%) for varenicline compared with placebo (2.4%) in the non-psychiatric cohort. Rates of neuropsychiatric side effects in bupropion (2.2%) and nicotine patch (2.5%) cohorts were similar to placebo. In fact, the only completed suicide among the entire 8144 participant study over 24 weeks occurred in the placebo cohort of the

Table 1 Summary of smoking cessation regulations among civilian and military populations

	Civilian (FAA) [21]	US Air Force [22]	US Army [23]	US Navy [24]
General guidelines	- Requires documentation of use, name and dosage of medication and side effects - Off medication for at least 30 days and no side effects	- No general guidelines	- Treat for 8–12 weeks; consider stopping after 7 weeks if not abstinent	- Only NRT may be used during flight
NRT	- No specific regulation	- Inhaler approved while not flying	- Grounded* for initial 72 h of treatment - Grounded for any smoking relapse until cleared by FS - No gum while flying; patch allowed in flight	- Grounded for initial 48 h of treatment with patch - Enrolled in formal organized stop smoking program - Duration does not exceed 3 months
Bupropion	- No specific regulation	- Use in smoking cessation not approved	- Grounded for initial 2 weeks of treatment - Maximum dose 300 mg daily	- Grounded for duration of treatment, plus 2 weeks
Varenicline	- Not approved for active use	- Use in smoking cessation not approved	- No regulation	- Grounded for duration of treatment, plus 1 week

FAA Federal Aviation Administration, FS flight surgeon, NRT nicotine replacement therapy. *Grounded, restricted from flight duties non-psychiatric study arm. The most frequent adverse events by treatment cohort across the trial were nausea (varenicline, 25%), insomnia (bupropion, 12%), abnormal dreams (nicotine patch, 12%), and headache (placebo, 10%). In summary, this largest study to date comparing the three primary smoking cessation medications found that varenicline, bupropion, and nicotine patch are all superior to placebo without worse neuropsychiatric side effect profiles, whereas varenicline is both superior to the other two active medications and with a lower rate of neuropsychiatric side effects compared with placebo in a cohort of participants without comorbid psychiatric illness. In response to this study, the FDA removed the black box warnings about mental health side effects from varenicline and bupropion in December 2016 [26].

Conclusion

While cigarette smoking is clearly hazardous to the health of members of the general population, this review has attempted to highlight the unique hazards to military and civilian aviators of smoking, nicotine withdrawal, and smoking cessation medications to include NRT, bupropion, and varenicline. Civilian aeromedical examiners and military flight surgeons therefore have a difficult job of balancing risks associated with both smoking and smoking cessation in treating and certifying aviators for flight duty. We believe, however, that current regulations may be too conservative in limitations placed on smoking cessation therapies: particularly given the almost complete lack of regulations related to smoking and unassisted nicotine withdrawal in aviators. While NRT is generally accepted in flight in the Army and Navy following a brief grounding period to account for initial nicotine withdrawal during a quit attempt, justifying bupropion and varenicline use is very difficult in all US aviators given current regulations. Yet as discussed above, varenicline in particular may actually lead to better success with fewer side effects than either NRT or even placebo. An evidence-based regulation might therefore allow for expanded use of this medication during flight, though perhaps still allowing for a brief initial grounding period as with NRT use in some services.

One limitation of this review is a focus on cigarette smoking, given the unique effects of CO as described above. Within the military in particular, however, smokeless tobacco use is actually higher than seen in the civilian population [2]. Moreover, many former-smokers have transitioned to e-cigarette use, with relatively low prevalence of quit attempts in this population [27]. Data from 2015 to 2016 among US Navy aviators found that 9.3% currently used e-cigarettes at the time of the study, while a surprising 31.4% admitted to having ever tried e-cigarettes [28]. While e-cigarettes may avoid many of the complications specific to CO in traditional cigarette smoking, the known effects of nicotine intoxication and withdrawal discussed above nonetheless necessitate increased research into smokeless tobacco and e-cigarette use among aviators.

Medications prescribed to treat tobacco use disorder rightly receive intense scrutiny within the aviation medicine community. Yet the risks of these medications should not automatically be given greater weight than the risks associated with cigarette smoking, smokeless tobacco, and even untreated nicotine withdrawal in the absence of data justifying such conservative limitations on these medications. With a renewed emphasis on treating dependence to nicotine in all forms, including potentially loosening current aeromedical regulations to make quit attempts regulatorily easier for aviators, flight surgeons and other aeromedical examiners can simultaneously improve the health of aviators while ensuring the safest possible flight environment.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Disclaimer The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army, the Department of Defense, or the US Government.

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