We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Physiologic Challenges to Pilots of Modern High Performance Aircraft

Douglas Summerfield, David Raslau,
Bruce Johnson and Lawrence Steinkraus

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.75982>

Abstract

Fourth generation aircraft, such as the McDonnell Douglas F-15 “Eagle,” and the fifth generation platforms that followed, including the Lockheed Martin F-22 “Raptor,” pose unique physiological challenges to arguably the most important “system” on the aircraft, the human. Advances in aeronautical engineering have enabled next-generation aircraft to operate well beyond the natural limits of human endurance. Although the demand for unmanned systems is increasing exponentially, continued use of manned aircraft is still desirable within civilian and military operations for various safety and security reasons. With the continued presence of pilots in cockpits, future aircraft designers will require a basic understanding of the unique physiological factors affecting human performance in this domain. Given knowledge of human limitations, strategies for real-time on board monitoring of the “human system” may be employed to increase the safety of the pilot and aircraft.

Keywords: fifth generation aircraft, aerospace medicine, acceleration atelectasis, future of manned flight, human cockpit monitoring

1. Introduction

Aerospace Medicine is a sub-specialty within the broader Occupational Medicine discipline, requiring licensed physicians to complete specialized training to ensure and enhance the health, safety, and performance of individuals exposed to air and space operational settings. Unique hazards in these environments include exposure to microgravity conditions, various radiation sources, multi-axial G-forces, and hypoxic conditions, among others. Aerospace medicine practitioners often further specialize in niche aspects of aerospace medicine, applying

human performance enhancement (HPE) and human systems integration (HSI) tenets to both hyperbaric environments (dive medicine) and hypobaric disciplines (space medicine, high-altitude wilderness medicine). Additionally, some specialize in human dynamics; focusing on highly integrated “man-machine” challenges such as high-performance aircraft and ejection seat emergency escape technologies [1]. As human factors specialists, Aerospace Medicine specialists are ideally suited to participate in the development of new life-support systems in modern aircraft. Unfortunately in recent times, there appears to be a decrease in the medical role during initial design and testing, leaving medical specialists scrambling to make sense of new physiologic ailments after an aircraft has become operational. This has not always been the case. This chapter will address emerging challenges to human health in modern “next generation” fighters as well as ways in which engineers and aerospace medicine professionals may address them.

1.1. Brief history of aerospace medicine

Scientific interest in the effects of human and animal exposure to high-altitude environments can be traced to the observations of Father Jose de Acosta in the late 1590s, more than 300 years before the Wright brothers first flew their *Flyer* among the dunes at Kitty Hawk, North Carolina. Evaluating the Andes high-altitude mountainous environment, Father Acosta surmised the thin “element of air” was causing animals and humans to become ill [2]. Decades later, in 1643, Evangelista Torricelli created the first experimental vacuum. In honor of his accomplishments physical units of pressure were named after him and are known as torrs [3]. Later, Robert Boyle of “Boyle’s Law” fame, described the first case of decompression sickness when he observed bubble formation in the eyes of a viper exposed to vacuum environments [4].

Research on the physiologic responses specific to flight took place among early balloonists. On September 19, 1783, brothers Joseph and Etienne Montgolfier sent aloft a duck, a rooster, and a sheep to elucidate hypoxia-like effects on mammals [5]. Unfortunately, shortly thereafter in 1783, researcher Jacques Charles, of Charles’ Law fame, endured the first aviation mishap. While piloting a balloon, his passenger unexpectedly exited the basket, thus lightening the balloon and triggering a rapid ascent to an approximate altitude of 10,000’ MSL, causing Charles to experience ear and sinus pain [6]. Even one of the United States’ founding fathers, Benjamin Franklin, took an early interest in high altitude research when he asked early balloonist Dr. John Jeffries to take his pulse during a flight. Jeffries noted that his pulse increased from 84 beats per minute (bpm) at sea level, to 92 bpm at an altitude of 5812’ MSL [7].

Regrettably, the first fatalities in aviation occurred on June 15, 1785 when Pierre de Rozier and Pierre Romain unsuccessfully attempted to pilot a balloon across the English Channel. Thirty minutes after takeoff their balloon caught fire, killing both of them. Interestingly, this event also witnessed the first ground casualty, although not as a direct result of impact; De Rozier’s fiancée, who witnessed the event, subsequently collapsed and died. Other notable medical incidents occurred during early balloon flights including the first in-flight emergency (IFE) when, on March 7, 1809, John Pierre Blanchard experienced a cardiac arrest, otherwise known as a “heart attack,” while piloting his balloon. During the episode, he fell from his balloon from a height of approximately 50’, dying a year later from his related injuries [7].

One of the early grandfathers of Aviation Medicine was French physiologist Paul Bert. He trained in engineering, law, physiology, and medicine. His work included experiments demonstrating oxygen toxicity on animals as well as the therapeutic nature of oxygen in relieving symptoms found in balloonists at altitude. In 1878 he wrote *La Pression Barometrique, Recherches de Physiologie Experimentale*, which was so comprehensive it was later translated into English and used by early aerospace physicians during World War II [4, 8].

The Wright Brothers, with their successful flight on December 17, 1903, ushered in the age of powered heavier-than-air flight. Within 5 years, on September 17, 1908, the first passenger died in an aircraft accident. Orville Wright was demonstrating the latest model of the Wright Flyer to the US Army when the right propeller broke in flight leading to a stall and crash. The passenger on that flight was Army Lieutenant Thomas Selfridge who suffered a skull fracture. Despite attempts at early neurosurgery, Lt Selfridge died 3 h later. Orville himself suffered four broken ribs, a broken thigh, and a dislocated hip. It was felt that Lt Selfridge may have survived had he been wearing head protection and as a direct result of this accident, one of the first human safety measures in aviation was employed: the use of a helmet [9]. Later, after all six of the Wright model C aircraft, which the army had purchased, crashed, further engineering safety measures were taken by the US Army. An investigation board felt that “pusher” type aircraft were more unstable and a crash would result in the engine, which was situated behind the pilot, coming forward and crushing the aviator. Subsequent US military aircraft of the era had engines in the “tractor” configuration [10].

Aside from aircraft design, advances in pilot selection began to make aviation safer. Pre-war aviators often were those found to be unfit for the infantry. Even early in World War 1 “soldiers disqualified for further combat because of battle fatigue, shell shock ... became pilots.” The end result was up to 42% of aircraft losses and deaths may be caused by “human factors” [11].

In this setting Dr. Theodore Lyster appeared. Dr. Lyster is considered by many to be the “Father of Aviation Medicine.” An American Army doctor, he arrived in Europe in December of 1917 and spent 3 months studying pilots and conditions affecting their performance. He then returned to the United States and established the Air Service Medical Research Lab on Long Island which had a hypobaric chamber. He developed new medical standards for the US Army Air Corps. In addition it was Dr. Lyster who first introduced the term “flight surgeons” when describing physicians who specialize in caring for aviators, and he was instrumental in ensuring that flight surgeons were part of each flying unit and would deploy with their squadrons rather than being assigned to a separate larger medical command [12]. This practice is still in place today in the United States military where an assigned flight surgeon is an integral part of each squadron.

Despite these new standards set by Dr. Lyster, it seemed as if the medical and aviation communities were in a perpetual battle between standards that were too rigid and aviators who excelled despite physical defects which would have otherwise grounded them. One famous civilian who personified this was Wiley Post who lost his eye in an oil rig accident early in his aviation career. He subsequently went on to become the first pilot to solo around the world, discover the jet stream, and he created the first practical pressurized suit for high altitude flying [13].

Additional examples of highly skilled pilots who did not meet the current medical standards are found in World War 1. One of the most famous American units to fight in the war was the Lafayette Escadrille. These flyers, several of whom obtained the unofficial title of “Ace” after downing five enemy aircraft, were hard worn by their combat service. Many of the members could not meet the Army Air Corps medical standards. Raul Lufbery, the triple Ace, was “over-age, had rheumatism, and could not walk a straight line backwards.” Others had poor vision, color blindness, and injured extremities. Eventually these pilots would be granted special approval so their valuable experience would not be lost in a fledgling service so in need of experienced veterans [14].

The controversy continued into World War 2, where one can find any number of stories of aviators “cheating” at their eye exam. This includes Robert Morgan who would later pilot the “Memphis Belle,” one of the first B-17s to famously complete all its required missions with its crew intact [15]. After the war Chuck Yeager broke the sound barrier with broken ribs after he fell from his horse, a condition which would have surely temporarily grounded him had he disclosed it to his flight surgeon [16].

In recent years, there has been a shift in the medical community from a restrictive approach, to the perspective of “how do we keep aircrew in the cockpit.” An example of this is seen in how NASA decided to return to space the well-known astronaut Story Musgrave after he underwent cataract surgery [17]. A further example is the United States Air Force’s lifting of restrictions on pilots who have had laser corrective eye surgery, or the fact that the Federal Aviation Administration (FAA) grants Special Issuances which by 2014 constituted 6% [18] of all certificates. It is with this mindset that the rest of the chapter is devoted, that of keeping the pilot in the cockpit even when technological advances push the limits of human endurance.

1.2. Current training and educational programs of aerospace medical personal

In the United States there is a wide array of education and training among the physicians who work in the realm of aerospace medicine. There are two primary tracks, military and civilian, with each track consisting of a “basic” and “advanced” level. The advanced levels of each track graduate medical specialists competent to become board certified in Aerospace Medicine under the purview of the American Board of Preventive Medicine.

In the military, physicians are referred to as flight surgeons. “Basic” flight surgeons attend their service’s specific primary courses, after which they are considered flight rated officers in the U.S. Military. Military flight surgeons have graduated medical school and have completed 1 year of post-graduate training, typically referred to as an intern year. Each branch of the military has different course requirements and duration to obtain “basic” flight surgeon status. The Air Force program consists of three courses of several weeks’ duration which include classroom training as well as civilian and military flight experiences. Students are exposed to hypobaric conditions using altitude chambers and those who fly with fighter aircraft are tested in centrifuges. Basic Army flight surgeon training is similar with an emphasis placed on rotary wing aircraft and Blackhawk helicopter simulations. The Navy program is substantially longer

and includes phases in which Naval flight surgeon candidates take basic ground school side by side with student Naval and Marine aviators, as well as significantly more “stick time” in both rotary and fixed wing aircraft. Regardless of the branch, all military flight surgeons are expected to fly with their assigned aircraft. In this way trust is built between the flight surgeon and his/her aviator patients, and the rigors of flight can be experienced firsthand, something which cannot be gained from medical books or classroom didactics (**Figure 1**). Physicians in the civilian sector who certify civilian pilots under Federal Aviation Administration (FAA) guidelines are referred to as Aviation Medical Examiners (AMEs). These are physicians trained and designated by the FAA to certify pilots’ medical certificates. Physicians can be trained in any specialty with the requirement that they attend a 1-week course with refresher training every 36 months [19].

Advanced training in Aerospace Medicine leading to board certification is significantly longer than civilian or military basic courses and lasts 2–3 years depending on the program. These programs include the Air Force program located at Wright-Patterson Air Force Base, the Army program at Ft. Rucker in Alabama, and the Navy program located at Pensacola, FL. The civilian programs are located at the University of Texas-Medical Branch in Galveston, TX, and the Mayo Clinic in Rochester, MN [20]. All programs require completion of an MD or DO degree and at least 1 year (internship) in clinical care. In addition, most programs require students to obtain a Masters in Public Health during their time spent in training. Although there is naturally some overlap in topics covered, the programs then diverge in their education to focus on the specific needs of the respective military or civilian populations.

Military training focuses on a typically younger, healthier population that works with high-performing aircraft in challenging training and combat situations. Therefore a variety of training is needed including learning the flight environment, broad clinical experience, and even accident investigation. In addition, aerospace trained physicians in the military will also

Figure 1. United States military flight surgeons are mandated to experience the rigors of flight to better understand the physiologic demands placed on their aircrew patients. The rise of single-seat only aircraft are challenging the abilities of these medical professionals to diagnose and treat new ailments seen in modern fighter-type aircraft.

take care of family members of the aircrew, which expands the requisite medical knowledge needed for competent care.

The civilian programs focus on care for the civilian aerospace communities (commercial and private pilots, Air Traffic Control, etc.) and, more rarely, space crew and passengers. As mentioned previously, there has been a shift in medical evaluations from a restrictive approach to developing standards for safe return to flight after adequate medical evaluation and treatment. Therefore, there is a strong emphasis on clinical experience and working closely with the Civil Aerospace Medical Institute (CAMI) division of the FAA. In the case of space crew members or passengers, training is coordinated with NASA, private agencies, and the FAA.

With increasing numbers of single-seat aircraft it is becoming harder for flight surgeons to actively participate in this unique environment (**Figure 2**). Fifth generations aircraft such as the F-35 and F-22 are all strictly single seat aircraft. When these modern aircraft have been associated with unusual and unexpected health concerns for their pilots, it has been more challenging for flight surgeons to diagnose and treat these problems since they cannot experience these conditions for themselves. A small cadre of military pilot-physicians exists, and they have been useful in human-machine risk assessment and mitigation approaches, but most flight surgeons serving high performance aircraft operations are limited in their ability to directly observe flight operations, and this has hampered investigations.

Figure 2. Advanced training in Aerospace Medicine may include further hands on exposure in high performance aircraft. Here, a United States Air Force Resident in Aerospace Medicine undergoes training in the T-6 Texan II aircraft with an instructor pilot during Medical Officer Flight Familiarization Training.

2. Decompression sickness in extreme high altitude aviation

2.1. Current cabin pressure control and mitigation strategies

Due to the altitudes flown by many high performance aircraft, cabin pressurization is important for a number of reasons. These reasons include hypoxia, hyperventilation, extreme temperature changes, as well as expanding trapped gasses and the risk for decompression sickness. Thus the need for protecting the pilot from stressors in the hypobaric environment is imperative.

Two physiologic responses to high altitude, hypoxia and hyperventilation, share similar symptoms and can be confused for one another. This confusion can make it difficult for aerospace medicine professionals as well as aircraft designers to determine the underlying cause of a pilot's symptoms. These symptoms include muscle cramps, paleness, and cold clammy skin. There may also be changes in mental status which can make a pilot's recall of the event difficult.

The interactions between hypoxia and hyperventilation are as follows, with the caveat that hyperventilation can also be brought about by other causes such as heat, air sickness, positive pressure breathing, and psychological stressors such as fear and anxiety. In brief, lower pressures lead to lower partial pressures of oxygen and increase the risk for hypoxia. Hypoxia in turn will increase respiratory rate, thus causing hyperventilation. With the increased respiration rate, blood CO₂ levels fall which in turn change pH. Changes in blood pH and CO₂ levels may lead to many of the symptoms and can negatively impact cerebral blood flow and thus a pilot's ability to process information and make decisions or react to emergencies.

Different strategies are employed to maintain cabin altitude in order to decrease the risks of high altitude and maintain pressures which are more tolerable for humans. These include isobaric, constant differential, and a sealed capsule. Modern airliners utilize an isobaric mode of pressurization, typically after reaching 6000–8000 ft. Any further increase in altitude beyond the predetermined altitude will not result in a corresponding change in cabin pressure. High performance aircraft on the other hand generally employ a constant differential strategy that maintains a constant pressure difference between the atmosphere inside and outside of the cabin. One advantage for military use with the latter system is, by allowing a higher cabin altitude, less catastrophic results may occur from damage incurred during battle, such as a damaged canopy which would lead to a major pressure breach.

Cabin pressure has typically been maintained by diverting high pressure “bleed air” from the aircrafts engines, cooling the air, then instilling it into the cabin. Since air is continually entering the cabin, it also needs to be released via a pressure valve. Thus aircraft cabins are not air tight and a continual supply of fresh air should always be entering the cabin. Unfortunately, flaws in the bleed air system have proven to be fatal. In 2010 an F-22 crashed in Alaska after an overheating engine caused the bleed air environmental control system and the onboard oxygen generating system to shut down [21]. The widow of the pilot filed suit against the major manufactures of the aircraft and eventually settled litigation. Interestingly the

lawsuit stated that the system was built “without adequate backup safety measures or proper sensors to warn the pilot if there is a problems” [22]. Of note, the Boeing 787 was designed to maintain cabin pressurization using electrical pumps versus bleed air systems. Whether this approach will be introduced in high performance aircraft remains a question.

2.2. U2 and other airframe exposures

Exposure to high attitude carries with it a significant risk of decompression sickness (DCS). DCS is thought to occur when inert gasses, primarily nitrogen, come out of solution within tissues at low barometric pressure. In aviation, the first reported cases occurred in high altitude balloons in the 1930s. The risk for DCS can be reduced for altitudes of 18,000–43,000 ft by breathing 100% oxygen prior to ascent for short exposure times of 10–30 min. This has the advantage of “washing out” excess nitrogen. Staying on 100% oxygen is required in flight if exposure to these altitudes is continued. Risk factors for DCS include physical activity at altitude, repeated exposures to altitudes greater than 18,000 ft, prior history of DCS, faster rates of ascent, alcohol consumption prior to ascent, persons with higher body fat, and scuba diving prior to flight. There is also some thought that increased age as well as prior long bone injuries put one at risk [23].

DCS is broken down to Type 1 or Type 2. Type 1 is less serious and involves musculoskeletal and skin illness, classically referred to as the “bends” and “creeps” respectively. Type 2 is more serious and involves neurologic and cardiopulmonary disease, the latter which is termed the “chokes.” Neurologic symptoms range from dizziness, ringing in the ears, numbness, bladder incontinence, and inability to walk, to seizures, coma, and death [24]. According to research conducted by the Air Force Research Laboratory (AFRL), descent from high altitudes to ground level is an effective treatment for altitude DCS. The majority (95%) of DCS sufferers who were tested at the AFRL were treated with ground level oxygen and saw a rapid decrease in DCS symptoms, while the remaining individuals were given hyperbaric treatment. Descent is an effective treatment method because DCS is caught early through crew monitoring in the controlled environment at the AFRL. During actual operations, it is likely that a higher percent of DCS sufferers would need hyperbaric treatment [25].

It was well known for years within the Flight Surgeon community that some pilots of high altitude aircraft were experiencing signs and symptoms consistent with decompression sickness and these were often underreported. This was particularly true in the Lockheed U2 community. In the past decade, pilot and researchers have been more open and a number of studies have been performed on U2 pilots as well as personnel who work as safety monitors inside altitude chambers. Excellent work by McGuire and colleagues has now been published in a number of studies. These studies report brain changes with repeated exposures to hypobaric normoxia. Specifically U2 pilots and altitude chamber staff have white matter changes which are seen on MRI [26, 27]. These changes have been linked to diffuse axonal injury [28] and those with a higher burden of white matter changes score lower on neurocognitive tests when compared to other pilots [29]. All these changes were linked to hypobaria without hypoxia, thus it seems low pressure itself may be a risk for permanent changes in the brain which can lead to subtle cognitive decline.

Future aircraft may go higher and even skirt the edges of space. Thus careful consideration needs to be given for aircrew protection. U2 pilots are equipped with a pressure suit, however as seen above, neurocognitive changes may already be occurring. One possible explanation may be that most pressure suits do not provide the wearer with a full 1 ATM of pressure, due to the need for a flexible suit, thus the pilot is exposed to hypobaria.

As opposed to chronic repeated exposures to hypobaria, acute exposure to high altitude, such as a rapid decompression, has its own set of problems. During acute exposure aircrew have a limited amount of time to institute measures to save themselves. This is termed “Time of useful consciousness” or TUC for short. Intuitively the higher an aircraft is, the less time is available for a pilot to save himself. By 50,000 ft an aviator only has between 9 and 12 s before they become unconscious (**Table 1**) [30]. Factors such as exercise and smoking will even further decrease that amount of time.

At the altitude of Armstrong’s Line, 63,000 ft, pressure is so low that water boils at body temperature (37°C), although due to the strength of skin in practice this typically does not occur at that level. Above that level the process of ebullism may occur, gas bubbles forming within bodily fluids. There have been accidents which have occurred at these altitudes, although not within fighter aircraft. Most recently the crew of the Space Shuttle Columbia died from this phenomenon. Although they were wearing pressure suits, none were able to close and lock their visors prior to incapacitation and some had their gloves off, thus limiting the protection received by the rest of the suit. Surprisingly exposure to these altitudes is survivable if caught and treated quickly enough. In 1966 a spacesuit technician working in a ground based chamber was accidentally exposed to the equivalent of 120,000 ft. He is reported to have felt the saliva “boiling” off his tongue as he passed out. He regained consciousness at 14,000 ft as he was repressurized. Amazingly he suffered no neurologic sequelae and did not even require hospitalization. In 1982 another ground based chamber accident exposed an individual to 73,000 ft for what is believed to be 1–3 min. After a 5-h hyperbaric recompression, he survived. More amazingly a 1-year follow-up revealed no neurologic abnormalities [31].

Altitude	Time of useful consciousness
18,000	20–30 min
22,000	10 min
25,000	3–5 min
28,000	2.5–3 min
30,000	1–2 min
35,000	0.5–1 min
40,000	15–20 s
43,000	9–12 s
50,000	9–12 s

Table 1. Time of useful consciousness “TUC” is the amount of time aircrew members have to institute life saving measures before they are incapacitated after acute exposure to the hypobaric conditions of high altitude.

Current fighter aircraft have been reported in the lay press to operate at extreme high altitude, although likely below the level of the Von Karmann line, which is at 47 miles and is the level at which the atmosphere is too thin for aerodynamic surfaces to control the direction of the aircraft. As fighter aircraft go higher and higher, the very real possibility of aircraft operations in the early reaches of space exist. With this in mind, systems which automatically detect cabin or “space suit” pressures may be needed. In the event of a pressure breach, either through accident or combat, there is mere seconds for a pilot to react. The life of the pilot and the aircraft itself may be saved by an “automated” copilot within the aircraft. This would necessitate a computer system taking over should there be a breach in the pressure system and the pilot not responding to an automated computer generated inquiry.

3. Acceleration, G-forces, and countermeasures

3.1. Brief explanation of G_x , G_y , G_z

During flight, acceleration and changes in vectors can cause changes in the amount of gravitational force that is experienced by a pilot. These can be positive (increased force) or negative (decreased force). Pilots feel forces acting on their bodies is in the opposite direction of the actual force vectors. This can be somewhat confusing so convention sets the positive directions of the acceleration forces. Unfortunately, multiple conventions are used which can further add to the confusion [32]. No one convention is better than another. One commonly used convention is the “right hand rule” (**Figure 3**). The pilot holds his right hand and fingers as indicated in the figure and the fingers then point in the positive direction of each force, $+G_x$ in the direction of the pointing finger, $+G_z$ in the direction of the thumb, and $+G_y$ in the direction of the middle finger.

Another way to think about acceleration forces is to think about how the eyes would move in response to the given acceleration [32]. When the pilot is experiencing $+G_x$ it is referred to as “eyeballs in,” and $-G_x$ is referred to as “eyeballs out.” One of the advantages of this convention is that it leaves little room for error since the experience of the pilot is exactly what is described.

3.2. Human limitations

There are limits to how much acceleration force the human body can tolerate. Tolerance depends on several factors including the magnitude of the acceleration force applied, direction, and duration as well as subject factors including age, weight, height, and blood pressure [33, 34]. Tolerance is somewhat subject to training, and there is wide variability between individuals. In addition, other factors can affect tolerance of G-forces including medical conditions, medications, and use of other substances (such as alcohol).

Despite the high number of variables that contribute to tolerance, one of the most important factors remains the direction of the acceleration force. Each axis has its own specific limitations in the positive and negative directions. For example, humans can tolerate >10 G in the $+G_x$ direction while only about 2–3 G in the $-G_z$ direction. This is due to the fact that there are

Figure 3. The right-hand rule. This figure demonstrates the “right hand rule” convention of G-force direction. The pilot holds his right hand and fingers as indicated in the figure and the fingers then point in the positive direction of each force, +Gx in the direction of the pointing finger, +Gz in the direction of the thumb, and +Gy in the direction of the middle finger. As an example, when a pilot experiences +Gx (which is pushing forward) the sensation felt is that of being pushed into the seatback (drawing acknowledgement Iaswarya Ganapathira, D.O.).

physiologic compensatory mechanisms to increase blood flow to the brain but none to prevent excess blood flow.

There are also different terms used to describe various aspects of G-force intolerance. “Gray-out” describes when vision loses hue and vision appears to be more gray. Tunnel vision describes the progressive loss of peripheral vision. “Blackout” is the complete loss of vision while still maintaining consciousness. “A-LOC” stands for “Almost Loss of Consciousness” and “G-LOC” describes a G-force induced loss of consciousness. “Red-out” describes the reddening of vision from negative G-forces which drive the lower eyelid into the field of vision.

3.3. Current countermeasures

Excessive G-forces may result in a sufficient reduction in blood flow to the brain such that G-LOC ensues. G-LOC can be and have been catastrophic and countermeasures have been developed to try and prevent G-LOC.

Physiologic countermeasures include physical training to improve overall fitness, cardiovascular function, positive pressure breathing for protection against G, and the anti-G straining maneuver [35]. These measures employ physical techniques to improve G tolerance. They can be helpful but have limitations as well.

Mechanical countermeasures revolve around the anti-G suit, positive pressure breathing (PPB), and (theoretically) cockpit design. During World War 2, Dr. Earl Wood was working as part of a laboratory team located at the Mayo Clinic charged with finding ways to improve G-force tolerance of pilots (**Figure 4**). Their work led to the development of the anti-G suit. The conventional “suit” is worn like trousers and, with the aid of a weighted valve, inflates when G force is above 2G. This compresses the lower extremities and abdomen using air bladders promoting return of blood back to the heart and head (**Figure 5**). Newer versions of the anti-G suit add higher G-force protection [36]. PPB works by assisting pilots to maintain oxygenation when G forces and constricting chest garments work to restrict chest movement and lung expansion. Wood et al. recommended changes in cockpit design to maximize G tolerance, recommending prone position as the best solution. An attempt to improve G tolerance by canting the seat backward was done in the F-16, and while appearing logical, was not supported by centrifuge testing. All recent high performance jets now place the pilot upright in the cockpit [37].

As more advanced aircraft have been created which test the boundaries of human tolerance, there has been ongoing interest in developing more advanced anti-G systems. One of these is the Advanced Technology Anti-G Suit which confers effortless protection up to +9 Gz and consistent protection up to +12 Gz with additional straining [38].

A new challenge for pilots in fifth generation aircraft is multi-axis acceleration wherein thrust vectors may be variable allowing increased aircraft maneuverability. G forces in these aircraft are likely to be multi-axis versus simple Gz or Gx forces. Effects on pilots remain investigational, with research ongoing in specially constructed centrifuge facilities [39].

Figure 4. Dr. Earl Wood (on the right, wearing a white lab coat) is working in the Mayo Clinic centrifuge laboratory to help develop the G-suit.

Figure 5. Dr. Earl Wood is standing next to a display case exhibiting the G-suit he helped develop.

4. Acceleration atelectasis

4.1. Alveolar collapse under acceleration and increased oxygenation concentrations

Acceleration atelectasis is an old condition which has become new again. In healthy lung tissue, the smallest unit in the lung is the alveoli. These tiny sac-like structures are delicate and as described by John West in west's lung zones, blood flow through each region of the lung is influenced by gravity. Typically at the end of expiration the pressure in the alveoli is within 2 mmHg of atmospheric pressure. Current thinking of the pathophysiology of acceleration atelectasis is, under conditions of high G forces and high increased fraction of inhaled oxygen, alveolar collapse occurs in the dependent regions of the lung. This collapse can cause chest pain, shortness of breath, and cough [40].

Tacker and colleagues found that atelectasis, alveolar collapse, can be exacerbated by three conditions: the use of 100% oxygen, +Gz, and even by the anti-G suit itself. In their study Tacker exposed 12 subjects to aerial combat maneuvers under a range of forces spanning from 4.5 to 9 G. They found that above 5 G up to 50% of the pulmonary airways were in some way distorted and even closed. This distortion of the alveoli led to a reduction of up to 20% of the vital capacity, the greatest volume of air which can be exhaled after taking the largest possible breath, in the research subjects. The G-suit itself may further exacerbate the problem by elevating the diaphragm, thus decreasing vital capacity through extrinsic compression of pulmonary space [40].

The use of high inspired oxygen percentages requires explanation. Prolonged high levels of oxygen have long been shown to be detrimental to ICU patients or those undergoing anesthesia, likely due to another condition known as absorption atelectasis. Absorption atelectasis reflects the fact that the human respiratory system is so efficient at absorbing oxygen that it can be taken up more rapidly across the alveolar-capillary membrane than what can be delivered to the alveoli during normal pressure respiration [40, 41]. When the United States Air Force

developed the On Board Oxygen Generation System (OBOGS), Haswell and colleagues found a significant reduction in vital capacity at inspired oxygen concentrations above 70%. Haswell noted “Given the unpleasant nature of the respiratory symptoms and the absence of knowledge about the effects of repeated development of acceleration atelectasis, limiting oxygen concentration ... seems worthy of consideration” [42].

This reduced vital capacity could be alleviated by a cough, deep breath, or anti-G straining maneuver. Both Tacker and Haswell found the reduction in vital capacity could be relieved by positive pressure breathing at 30 mmHg. It is worth noting that standard patient ventilator practices in modern intensive care units limit the use of inspiratory pressures to “plateau pressures” less than 30 mmHg [40, 42]. As discussed later in this chapter, there is a need for continued research into this “old” concept of acceleration atelectasis.

5. Musculoskeletal injury and impact of life support systems and aircrew flight equipment

5.1. Neck injuries

Neck pain has been reported in up to 97% of all pilots [43]. Unfortunately the incidence varies tremendously as does its association with the type of airframe. A systematic review and meta-analysis of 20 articles conducted by Shiri and colleagues found no difference in the prevalence of neck pain, cervical disc degeneration, low back pain, or lumbar disc degeneration when they compared fighter pilots to helicopter or transport/cargo pilots. In the subset of high-performance pilots, they did however find that those who were exposed to higher G-forces were at a higher risk of neck pain, as were those that spent time looking over their shoulder in the “check-six” position [44].

There is disagreement regarding whether different models of high performance aircraft cause more neck pain. Some reports indicate as little as 18.9% prevalence of neck pain in F-16 pilots [45], while Verde and colleagues found an incidence of 48.6% in a small group of 35 F-16 pilots. This group had a much higher incidence than Eurofighter Typhoon pilots who only had a reported incidence of 5.7% in age matched controls. Verde speculated that the increased neck pain was secondary to the semi-recumbent seat position of the F-16 [46].

In F-15s, Chumbley et al. found a unique subset of neck pain and speculated it was due to cockpit layout. Similar to work done by Shiri, Chumbley found differences which may be attributed to the “check six” position. As part of their work which involved treating neck pain, Chumbley checked cervical range of motion and found rightward going cervical rotation improved after traction sessions. They speculated that F-15 pilots preferentially turned to the left due to cockpit layout, as the throttle is on the left side and slightly behind the stick which is placed center. In terms of treatment, Chumbley found that neck pain was statistically alleviated, when compared to controls, after cervical traction was applied to pilots after flying. The amount of cervical traction applied was roughly 10% of the pilot’s body weight [47].

In their literature review Chumbley and colleagues list proposed etiologies of neck pain experienced by high performance “fighter” pilots. These include high +Gz, rotation of the neck under +Gz (check-six position), fatigue, frequency of endurance training and physical exercise, and prolonged flexed posturing. From an equipment point of view, increasing the weight on the helmet may also place a pilot at risk. This is seen with the addition of night vision goggles as well as with the use of the Joint Helmet Mounted Cueing System (JHMCS). Countermeasures for the neck pain which have included strengthening and stretching exercises, spinal manipulation, and physical therapy have demonstrated mixed results, with spinal manipulation showing some promise [47].

5.2. Ejection seat injuries

In the early part of aviation history, pilots who found themselves in damaged or malfunctioning airframes had no real options to avoid impending death. Later, use of parachutes became common (though in WW 1 some services opted not to provide parachutes as they were worried pilots might leave their aircraft too readily) The challenge these pilots faced was how to escape the cockpit safely, either climbing or falling out when the situation would allow. In the jet age, one of the greatest advances in aircraft safety has been the ejection seat. Ejection seats are powered by rockets to expel the occupant from the cabin and away from the failing aircraft. Since time is of the essence in these situations, the rocket-propelled seat will violently eject the occupant. One common ejection seat, the ACES II, will reach 9-12G during the process which is significantly lower than other seats which could reach more than 18G [48].

Ejections seats, which were designed to save lives, have indeed accomplished that task. One manufacturer, Martin-Baker, keeps a tally of the pilots who have survived because of their ejection seats. In early 2017, their count was over 7500 lives saved because of their ejection seats [49]. However the use of ejection seats comes with the risk for potential bodily harm. Although injury is much more desirable than the alternative, efforts are still needed to focus on the prevention of injury to the extent that is possible.

One study looked at USAF injuries related to the use of ejection seats from 1981 to 1995. It was noted that injuries typically occurred in the head, neck, cervical spine, thorax, thoracolumbar spine, ribs, pelvis, and the upper and lower extremities. Injury rates were noted to be between 2 and 25%. Moreover, fatality was noted to occur in 0–11% [50]. Injuries can range from minor back strain that resolves on its own to as severe as a leg broken in 5 places. Continued work is needed in this area to preserve life and minimize injury.

5.3. Back injuries due to G-forces

Neck pain, as detailed above, and associated injuries are very common in aviation. Although the neck is the most susceptible area of the spine, G force-related injuries can occur along any aspect of the spinal column. Even in the controlled environment of centrifuge training, it is possible to sustain injury to the spinal column. One study assessed 991 subjects who were undergoing high G training in the centrifuge and found that 2.3% of them suffered from an

acute spinal injury [51]. In at least one case, the G-force from centrifuge training (which reaches up to +9Gx) was enough to cause a fracture in the lower spine in an otherwise healthy 32-year-old Flight Surgeon [52].

The addition of the highly stressful flight combat environment and more powerful aircraft increases the risk of injury. When the Japanese Air Self Defense Force introduced the F-15 Eagle into their fleet, there was a significant increase in musculoskeletal injuries related to the spine with 90% of surveyed pilots reporting pain [53]. There is some ongoing debate in the literature regarding how important these types of injuries may be and what impact they might have on the long-term health of subjects. One systematic review, which included 20 individual studies evaluating spine injury in pilots, found no statistically significant difference in back pain between pilots and non-flying personnel [44]. One possible interpretation of these conflicting pieces of information would be that ejection seats are indeed getting safer, and we are seeing improvement in back injuries. We would hope to see similar improvements in other areas as well.

6. Environmental factors

6.1. Noise

Measured in decibels (dB), sound is an auditory sensation in response to acoustic stimuli. Subjectively, any undesired sound is considered noise. Since the advent of heavier-than-air flying machines, both sound and noise remain inherent elements of manned aircraft operations, and modern high performance aircraft operations are no exception. While the majority of unwanted sound is generated by the power plant, several other sources of operationally innate noises include vibrations and sounds secondary to weapons system deployment. Regardless of the source, sound and noise exposures that exceed permissible exposure limits, as published by the Occupational Safety and Health Administration and the National Institute for Occupational Safety and Health, have the potential to result in injury.

Effects of noise on overall health have been studied. Deleterious effects have been seen in hearing, ringing in the ears, cognitive performance, and possibly even hypertension [54–57]. Although engineering can potentially mitigate much of external noises, there remains a need to relay critical information to the aircrew in the form of voice communication. This will place limits on the amount of noise mitigation that can be engineered into the system.

It is also important to distinguish between sound and noise exposures that aircrew experience while operating within a closed cockpit/flight deck versus the external environment experienced when approaching their aircraft while other aircraft operations are ongoing. As an example, the F-35A Lightning II is a fifth-generation fighter which has a measured aircraft ground noise level of 145 dB when the throttle is set to “Military Power” and 149 dB when set to “Afterburner” [58]. Obviously, the relative attenuation of the closed cockpit environment serves as an effective adjunct to triple hearing protection utilizing traditional earplugs in conjunction with the physical protection of a helmet and the acoustic protection of active noise-canceling technology. However, with the threshold of pain occurring around 120–

140 dB [59], it is reasonable to conclude that sound and noise considerations will remain critical in aircraft design and deployment as long as humans intend to work in or around them.

6.2. Vibration

Another factor that aircrew deal with is the vibrational forces created by the powerful machines at their command. One study looked at the effect of vibration on the ability to perform complex tasks and found that certain vibration patterns reduced cognitive performance [60]. Another study found that excess vibration can cause temporary hearing loss and impaired vision [61]. Another group studied vibrational effects and found that it reduced motion control [62]. In addition, airborne vibrations were found to cause symptoms of nausea, coughing, headache, and fatigue [63]. One of the most reported effects is that of back pain. It appears to affect rotary-wing aircrew more than fixed-wing aircrew as the former experience much more vibrational forces than the latter. Long term these effects may lead to chronic problems [64, 65]. Any of these adverse health effects could jeopardize safety and warrant continued efforts at mitigation.

6.3. Thermal stress

Another potential physiologic stressor to pilots is thermal stress. Humans are most comfortable in ambient temperatures ranging between 15 and 30°C [66]. There is the potential for cockpit temperatures to rise significantly above this comfortable range. Reports from pilots in the 1960s state that on hot days sitting on the steaming runway, temperatures in the cockpit climbed to nearly 60°C [67]. Even in 2015, it is still possible for cockpit temperatures to exceed 45°C. Sweating can unfortunately exacerbate the problem by increasing cockpit humidity and creating a greenhouse effect. The latest cooling systems try to adjust for humidity as well [68]. Additionally, systems malfunction and a pilot can become stuck inside the cockpit with the canopy down as occurred in an F-22 in 2006. The F-22 canopy system failed and was unable to be fixed or opened manually. Over the next 5 h, crews worked to cut off the canopy from the aircraft, during which cockpit temperatures rose throughout the extraction [69].

Thermal stress has significant implications aside from simple discomfort. Pilots report increased fatigue levels and decreased G-force tolerance under high thermal stress [70]. This can negatively impact performance and pose significant risk. Although efforts have been made to minimize the impact of thermal stress and improvements have been made, there remains ongoing concern in this area.

6.4. Toxins/fumes

Since the early days of aviation, toxins have impacted the health of both the aviator and the ground crew. Perhaps the most well-known of these is the reports of castor oil's effects on WW1 pilots. Although difficult to verify, castor oil *may* have been the cause of significant diarrhea in combat pilots. It is believed to have been thrown off by the engine and subsequently inhaled or ingested by the pilot sitting directly behind the engine [71].

One WW1 era toxin which has been confirmed is tetrachloroethane. For the ground crew, and those building WW1 aircraft, tetrachloroethane was found to cause significant adverse health effects, including death. It was used ubiquitously by all major combatants during the conflict as the varnish, also known as “dope,” to cover the fabric of the plane’s wings. Unfortunately reports after the war linked this toxin to at least 70 illnesses and 12 deaths. Many of the symptoms appear to have been hepatic/liver failure with transmission of the toxin through both inhalation and transdermal routes [72–75].

Although not next generation fighter type aircraft, there has been work within the commercial airline sector on this topic. In modern commercial aircraft, multiple volatile liquids exist in the various systems of an aircraft. Because air is circulated around the engine to be heated and pressurized, it is possible for cabin air to become contaminated with various fumes. There have been multiple reports from aircrew and passengers alike complaining of this occurrence. Symptoms associated with contaminated air include fatigue, dizziness, and anxiety [76]. More concerning is the increased rates of cancers, cataracts, and motor neuron diseases that may be associated with exposures, although at doses higher than would be expected in cabin air contamination events [77]. Despite the numerous concerns, investigations into cabin air quality of civilian airliners have repeatedly shown that the air quality on commercial flights is very good and there is no consistent exposure that should affect the general public. As Bagshaw, referencing cabin air quality, concludes in his article, “Aviation medical professionals throughout the world continue to monitor the scientific evidence and remain receptive to objective peer-reviewed evidence” [78].

In military aircraft, hydrazine is a specific example of a toxin which is of medical concern. Present in some current 4th generation fighters, such as the General Dynamics F-16 “Fighting Falcon,” it is used to power the emergency power unit (EPU) and is added to other rocket and jet fuels. Routes of exposure include inhalation, ingestions, or even absorption through the skin and eyes. Animal studies have shown liver damage and the potential for cancer formation [79, 80]. Exposure in humans can cause skin burns, dizziness, lethargy, vomiting, contact dermatitis, and conjunctivitis. Long term exposure has been reported in one case to lead to pulmonary edema, intestinal hemorrhage, liver necrosis, and death [81]. Due to the continued need for this potentially deadly material, the United States Air Force has instituted a multidisciplinary approach to dealing with this hazard. From the medical side, a surveillance program looking at labs such as baseline liver function is conducted on those potentially exposed. Furthermore the workers themselves are educated in minimizing exposure, safe handling when necessary, as well as the correct response to an accidental spill [82].

6.5. Radiation exposure: both natural and manmade

Radiation exposure is an area of ongoing concern. Typically our atmosphere protects us from most harmful waves from our sun or other sources of such as cosmic radiation. While operating at high altitude, there is less atmosphere to protect the aircrew and the job of protection falls to the windshield and skin of the aircraft, which may not be as adequate as hoped. One study estimated that pilots who fly for 56 min at 30,000 ft are exposed to the same amount of UV-A radiation as someone sitting in a tanning bed for 20 min [83]. However, as in other areas

this is controversial. For example, one study found no measurable increase in UVA/UVB/UVC radiation in flights at cruising altitude. Interestingly, UVA levels inside the cabins were actually lower than on the ground based upon the collected data [84]. Pilots have been shown to be at increased risk of other cancers including brain cancer and Hodgkin's disease [85]. However again, there is controversy regarding if cosmic radiation is solely responsible for this increased risk of cancer [86]. Another complicating factor is that sometimes there appears to be an increased risk of developing a cancer with no associated increase in the risk of death [87]. This raises questions of how clinically significant an increase in risk might be, whether a risk even exists, and whether it is important to address or not.

Design of aircraft cannot fully eliminate the exposure to higher levels of cosmic radiation during flight. Flight practices have changed allowing pilots to retire at a later age, thereby allowing a higher lifetime exposure. As such, we must continue to monitor the impact this has on pilot health and find ways to mitigate any adverse effects.

7. Current issues and controversies

7.1. Hypoxic-like incidents in modern jet fighters

As described above acceleration atelectasis is a pulmonary condition which was well known and described in the literature by the generation of Aerospace physicians active during the 1950s and 1960s. This "corporate knowledge" seems to have faded. A literature review conducted in 2017 on this topic in a major data base revealed only 15 relevant articles. Of these one article was speculative, one was historical, three were review articles, thus leaving only 10 articles. Furthermore these articles began in 1963 and ended with the last basic research article written by Tacker in 1987. Not included in this search was excellent work performed by Dr. J. Ernsting which was published in the 1960s. His research recommended up to 40% nitrogen for cabin altitude levels of 25,000 ft [88].

This older research has been revisited due to respiratory complaints reported in new fifth and some older fourth generation fighters. Most notably pilots of the United States Air Force's F-22 Raptor, a fifth generation stealth fighter, began to experience "hypoxia-like" symptoms in 2008. Due to the rising number of incidents and the subsequent fatal crash of an F-22 in November 2010, the F-22 fleet was subsequently grounded twice in 2011 [89]. After considerable effort to investigate possible causes, the problem was thought to be fixed after researchers came to believe the cause was effects of the upper body pressure vests on pilots' G-suits and narrow oxygen hoses [90, 91]. While the F-22 fleet was returned to flying, unfortunately problems have continued with "hypoxia-like" symptoms now seen in other aircraft. This has led to the grounding of both the newer F-35 Joint Strike Fighter as well as the United States Navy's T-45 jet trainer, an older aircraft [92, 93]. Problems have also been cited with the U.S. Navy's F-18 Super Hornet and the RAF Tornado, both of which use the OBOGS to supply oxygen to pilots.

Although the root cause of these symptoms was initially felt by some, including the United States Air Force Scientific Advisory Board, to be due to hypoxia, some experts have suggested

an alternative explanation including acceleration atelectasis. Indeed some of the symptoms reported by pilots, (cough, shortness of breath, chest pain) are very reminiscent of acceleration atelectasis [94, 95]. Other possible explanations put forth by renowned pulmonary researcher John West include reduced cerebral blood flow due to high +Gz, hyperventilation, CO₂ retention from increased work of breathing, decompression sickness, or even toxic fumes [94]. Regardless of the cause, both West and the USAF Scientific Advisory Board (SAB) have called for in-flight monitoring and warning systems.

7.2. Studying cognition in hypoxia

Loss of cabin pressure can occur quickly in rapid depressurizations or, more insidiously and dangerously, with gradual or slow depressurizations. United States military aircrews are taught to learn their individual symptoms by experiencing them first hand in hypobaric “altitude” chambers. When aircrew experience these symptoms, they are trained to react by going on 100% oxygen (“gang load” their regulators) to ensure their oxygen equipment is working correctly and when in doubt, to transfer to stored oxygen (“pulling the green apple”), descend to less than 10,000 ft, and communicate with the ground by declaring an in-flight emergency.

Due to the number of decompression sickness (DCS) incidents seen during such training, many military and civilian groups are now transitioning away from hypobaric hypoxia training in the altitude chamber toward normobaric hypoxia training which uses mixed gas to allow aircrew to experience hypoxic symptoms. While initially safer (fewer DCS events), this approach may lead to the potential that the symptoms experienced by the pilot in training may be different if those symptoms are due to hyperventilation during low pressure as opposed to hypoxia.

Additionally the concept of time of useful consciousness “TUC” is a somewhat crude and individually variable measure to describe the neurocognitive function of an aircrew exposed to high altitude. Researchers at Mayo Clinic are currently working on ways to detect subtle degradation due to hypoxia using other physiologic parameters, such as eye tracking, transcranial Doppler, ECG R-R’ variability, EEG, etc. [96] (**Figure 6**). After laboratory data are analyzed, future work will be needed to incorporate these findings into an aircraft in order to best support and alert a pilot to the possibility of slow cognitive decline way before TUC becomes an issue.

7.3. Studying cognition in high workload

Pilot workload in flying high performance aircraft has increased largely due to accelerating informational flows. Cockpits, while seemingly simpler in appearance, present multiple and layered details on the flying environment, navigational elements, mission specific data, and systems integration awareness items. Military pilots often are in contact with multiple ground, space, and aviation related resources. Warning systems often overlap or produce simultaneous alarms. Net-centric warfare allows for vast quantities of information to be readily available at the finger-tips of modern airmen. There may be a time in the near future when this information

Figure 6. Ongoing experiments at Mayo Clinic evaluating the physiologic responses which may be early signs of cognitive degradation during exposure to normobaric hypoxia.

is employed in such a way that a pilot in a manned aircraft would control a “squadron” of unmanned/drone aircraft. The primary processing center for these information flows is the pilot’s brain. In this setting it would be very advantageous to know the mental state of the pilot in terms of cognitive overload. Thus if one pilot was showing signs of cognitive decline, from any source whether it is due to overload or a physiologic even such as hypoxia, control of unmanned resources could automatically be passed to another manned system, or mitigation algorithms could assist the pilot to reduce overload or stressors.

There are a number of physiologic measures which have been shown to reveal a subject’s current cognitive load. These may prove useful if studied to define envelopes wherein performance predictions may be calculated and applied. While incapacitation is critical to detect, it would be better to detect degradation in the early phases to avoid incapacitation. Many of the monitoring and mitigation approaches have limitations which need to be understood if employed.

Relatively recent advances in eye tracking have linked subjects’ cognitive loads to pupil diameter in a variety of tasks such as sports and driving [97, 98]. Not only has pupil diameter shown to be a useful measurement, but so too does the amount of eye movement and even blink rates [99]. Because the eye muscles are the most sensitive muscle to oxygen depletion, eye tracking may also be a good indicator of hypoxia [100]. Limitations of eye tracking may

include difficulty detecting pupils during G-forces that may pull eyelids down thus obscuring the pupils. Also, due to the continual movement of a pilot's head, eye tracking may be better performed by a device which moves with head motions. This would suggest a likely location for an eye tracker to be on/in a pilot's helmet [101–105].

Aside from eye tracking, heart rate variability has been demonstrated by some to also correlate with physiologic reserve and potential cognitive stress. Each peak on an EKG is called the “R” wave. By measuring the distance between successive “R” waves, it has been found that the R to R interval continually changes. In fact there is more variability in young healthy individuals than those who are older and sicker. The latter have a more “fixed” interval with less variation. This decrease in variability has also been seen during increased cognitive load [106]. Further work would need to see if this can be practically performed regularly in flight.

Cognitive function measuring devices have included measurements of ocular saccades (rapid eye movements which change the point of eye fixation from one point to the next), EEG monitors, pupil size, and even eye blink velocity [103]. Practical use of these devices has been limited in the cockpit due to the technical issues such as difficulty of applying electrodes in the first case, bulkiness and reliability of devices and difficulty positioning sensors due to space limitations or changes in signaling under acceleration forces. Much more study is needed in this field but it is clear that in-flight monitoring will be an element in future manned flight.

8. Conclusion and the future of manned flight

An in-flight monitoring and warning system may be one way to safely keep “pilots in the cockpit.” One theoretical concept would be to monitor various physiologic parameters of the pilot. If physiologic parameters were found to fall outside of normal reference ranges, one could conceive that an auto-pilot would be activated and either takeover flying the aircraft completely or “ask” the pilot if it could assist. This could occur until the pilot was able to regain control, or it may need to “safely” eject the pilot and self-land the aircraft.

This may seem to be very futuristic, but similar technologies already exist. Although not directly measuring the pilot's physiology, newer block F-16s have begun to incorporate an auto-ground collision avoidance system (Auto-GCAS) as of 2014. This system compares the predicted flight path against the known terrain and institutes an automatic recovery if the two are predicted to touch. In an aircraft known to have increased risk for G-LOC, especially in new pilots, this system has already been credited with saving the lives of four pilots and their aircraft as of 2016. Future work is aimed at creating an Automatic Integrated Collision Avoidance System, which will also help prevent mid-air collisions [107].

Actual monitoring of a pilot's movement has been in place in combat aircraft for years via infrared beams. The Army's AH-64 Apache helicopter uses infrared sensors on either side of the pilot/gunner to detect movement of the pilot's head. This system is called the Integrated Helmet and Display Sight System, better known as IHADSS. It allows a computer to slew the

aircraft's gun to the pilot's monocle such that wherever the pilot/gunner is looking, the gun is pointed [108]. With a monocle already in place, one could also imagine an eye tracker looking back at the pilot to monitor the pilot's cognitive load and gradually assist in taking the workload off the pilot. It could do this by taking over critical systems of the aircraft, such as flying to avoid collision. Additionally it may even actively change displays in the cockpit in a manner which would help redirect the pilot's attention.

There are experimental research aircraft which currently employ some of these physiologic monitoring devices. At the University of Iowa's Operator Performance Laboratory, two Delfin L-29 jet aircraft are equipped with eye tracking devices as well as ECG monitors. Lead by Dr. Thomas Schnell, researchers there have developed software termed Cognitive Avionics Tool Set (CATS). This software imports on board data from physiologic sensors of the pilot in order to quantify human cognitive workload. Data analyzed include ECG, EEG, and eye tracking to name a few. Using CATS, operators on the ground can increase or decrease training scenarios based on how "overwhelmed" a subject is [109]. Further experimentation may be required to determine if cognitive decline due to hypoxia would also be detected by this system.

Currently the Royal Air Force (RAF) at the RAF Center of Aviation Medicine (CAM) also has jet aircraft with human physiologic monitoring capabilities. These aircraft are specially modified BAE Hawk T1 Mk1 aircraft, a platform similar to the U.S. Navy's T-45 Goshawk training aircraft. As a tandem aircraft, these jets are suited for research as the safety pilot-in-command operates the vehicle from the front seat while research subjects ride in the aft seat. Unfortunately, RAF CAM and its specially modified aircraft is scheduled to close by 2020 [110].

With all that has been discovered to date, there is also much more to be learned. By understanding current problems faced by pilots of 5th generation aircraft improved monitoring can take place. Monitoring can increase understanding of physiologic changes which occur as we push aircraft design into areas never before experienced by humans. By coupling monitors to automated systems which can "take over" when a pilot becomes incapacitated, human endurance can continue to be pushed to the limits in a safe manner.

Acknowledgements

The authors would like to thank Ms. Janice Duncan for help in compiling the manuscript and Iaswarya Ganapathira, D.O. for her illustrating skills.

This manuscript was funded in part by the Department of Defense, Mayo Clinic, and Dr. Paul Magelli.

Conflict of interest

The authors have no conflict of interests to declare.

Author details

Douglas Summerfield¹, David Raslau², Bruce Johnson^{3,4} and Lawrence Steinkraus^{5*}

*Address all correspondence to: steinkraus.lawrence@mayo.edu

1 Critical Care and Aerospace Medicine, Mercy Medical Center, Mason City, IA, United States

2 Aerospace and Internal Medicine, Rochester, MN, United States

3 Human Integrative and Environmental Physiology Laboratory, Mayo Clinic, Rochester, MN, United States

4 Cardiovascular Diseases, Preventive, Occupational, and Aerospace Medicine, Mayo Clinic, Rochester, MN, United States

5 Division of Preventive, Occupational, and Aerospace Medicine, Mayo Clinic, Rochester, MN, United States

References

- [1] Welcome to the Aerospace Medical Association [Internet]. Available from: <https://www.asma.org/for-the-public> [Accessed: Oct 1, 2017]
- [2] De Acosta J. Natural and Moral History of the East and West Indies 1604. Whitefish, Montana: Kessinger Publishing; 2003
- [3] Hack M, Vesel Z, Gariboldi L, Renshaw S, Ihara S, Fazlıoğlu İ, et al. Torricelli, Evangelista. Biographical Encyclopedia of Astronomers. New York, NY: Springer; 2007. pp. 1146-1147. DOI: 10.1007/978-0-387-30400-7_1390
- [4] Acott C. A brief history of diving and decompression illness. South Pacific Underwater Medicine Society. 1999;29(2):98-109
- [5] Davis JR, Johnson R, Stepanek J, Fogarty JA. Fundamentals of Aerospace Medicine. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2008. p. 2
- [6] The First Solo Flight: Jean-François Pilâtre de Rozier and the Marquis d'Arlandes [Internet]. 2009 Air & Space Magazine. Available from: <https://www.airspacemag.com/daily-planet/the-first-solo-flight-53893576/> [Accessed: Oct 1, 2017]
- [7] Davis J. Fundamentals of Aerospace Medicine. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2002
- [8] Bert P. Barometric Pressure: Researches in Experimental Physiology. Columbus, OH: College Book Company; 1943
- [9] Sept. 17, 1908: First Airplane Passenger Death [Internet]. Available from: <https://www.wired.com/2010/09/0917selfridge-first-us-air-fatality/> [Accessed: Oct 2, 2017]

- [10] Loening G. Takeoff into Greatness: How American Aviation Grew So Big So Fast. New York: Putnam; 1968
- [11] Jones D. Flying and dying in WWI: British aircrew losses and the origins of US military aviation medicine. *Aviation, Space, and Environmental Medicine*. 2008;**79**(2):139-146
- [12] Davis H. Generals in Khaki. Raleigh, North Carolina: Pentland Press Inc.; 1998
- [13] Elshatory Y, Siatkowski R. Wiley Post, around the world with no stereopsis. *Survey of Ophthalmology*. 2014;**59**(3):365-372. DOI: 10.1016/j.survophthal.2013.08.001
- [14] Miller R. Like a Thunderbolt: The Lafayette Escadrille and the Advent of American Pursuit in World War I. Washington, D.C.: Air Force History and Museums Program; 2007
- [15] Morgan R, Powers R. The Man Who Flew the Memphis Belle: Memoir of a WWII Bomber Pilot. New York: Penguin; 2001
- [16] Yeager C, Janos L. Yeager: An Autobiography. New York: Bantam Books; 1986
- [17] Mader T, Koch D, Manuel K, Gibson C, Effenhauser R, Musgrave S. Stability of vision during space flight in an astronaut with bilateral intraocular lenses. *American Journal of Ophthalmology*. 1999;**127**(3):341-343
- [18] Skaggs V, Norris A. Aerospace Medical Certification Statistical Handbook. Oklahoma City, Oklahoma: FAA Civil Aerospace Medical Institute, Administration FA; 2014. 2014 December 2015. Report No.: DOT/FAA/AM-15/22
- [19] Aviation Medical Examiner (AME) Training Federal Aviation Administration [Internet]. Available from: https://www.faa.gov/other_visit/aviation_industry/designees_delegations/designee_types/ame/ametraining/ [Accessed: Oct 1, 2017]
- [20] Residency Programs and Related Courses [Internet]. Available from: <https://www.asma.org/about-asma/careers/aerospace-medicine/residency-programs-related-courses> [Accessed: Oct 13, 2017]
- [21] Forces PA. Aircraft Accident Investigation: F-22A T/N 06-4125 JOINT BASE ELMENDORF-RICHARDSON ALASKA 16 NOVEMBER 2010. In: Force USA, editor
- [22] Settlement Reached in Haney F-22 Crash Lawsuit [Internet]. 2012. Available from: <https://www.flightglobal.com/news/articles/settlement-reached-in-haney-f-22-crash-lawsuit-375445/> [Accessed: Oct 1, 2017]
- [23] Brown J, Antunano M. Altitude-Induced Decompression Sickness. Oklahoma City, Oklahoma: Federal Aviation Administration, Civil Aerospace Medical Institute Aero-medical Education Division. AM-400-95/2; 1995
- [24] Signs and Symptoms of DCS [Internet]. Divers Alert Network. Available from: <https://www.diversalertnetwork.org/health/decompression/Signs-and-symptoms-of-DCS> [Accessed: Oct 1, 2017]

- [25] Krause K, Pilmanis A. The effectiveness of ground level oxygen treatment for altitude decompression sickness in human research subjects. *Aviation, Space, and Environmental Medicine*. 2000;**71**(2):115-118
- [26] McGuire S, Sherman P, Profenna L, Grogan P, Sladky J, Brown A, et al. White matter hyperintensities on MRI in high-altitude U-2 pilots. *Neurology*. 2013;**81**(8):729-735. DOI: 10.1212/WNL.0b013e3182a1ab12
- [27] McGuire S, Sherman P, Wijtenburg S, Rowland L, Grogan P, Sladky J, et al. White matter hyperintensities and hypobaric exposure. *Annals of Neurology*. 2014;**76**(5):719-726. DOI: 10.1002/ana.24264
- [28] McGuire S, Boone G, Sherman P, Tate D, Wood J, Patel B, et al. White matter integrity in high-altitude pilots exposed to hypobaria. *Aerospace Medicine and Human Performance*. 2016;**87**(12):983-988. DOI: 10.3357/AMHP.4585.2016
- [29] McGuire S, Tate D, Wood J, Sladky J, McDonald K, Sherman P, et al. Lower neurocognitive function in U-2 pilots: Relationship to white matter hyperintensities. *Neurology*. 2014; **83**(7):638-645. DOI: 10.1212/WNL.0000000000000694
- [30] Federal Aviation Administration. Introduction to Aviation Physiology. [Internet]. p. 3-3. Available from: https://www.faa.gov/pilots/training/airman_education/media/IntroAviationPhys.pdf [Accessed: Oct 23, 2017]
- [31] National Aeronautics and Space Administration. Loss of Signal: Aeromedical Lessons Learned from the STS-107 Columbia Space Shuttle Mishap [Internet]. 2014. Available from: <https://www.asma.org/asma/media/asma/Travel-Publications/NASA%20Shuttle/SP-2014-616.pdf> [Accessed: Oct 22, 2017]
- [32] Gillingham K, Wolfe J. Spatial Orientation in Flight. Texas: USAF School of Aerospace Medicine. Brooks Air Force Base; 1986. pp. 11-12
- [33] Voge V. Comparison of several G-tolerance measuring methods at various seatback angles. *Aviation, Space, and Environmental Medicine*. 1978;**49**(2):377-383
- [34] Burton R. Mathematical models for predicting G-duration tolerances. *Aviation, Space, and Environmental Medicine*. 2000;**71**(10):981-990
- [35] Protection Against the 'G' [Internet]. *Aviation Medicine: Aerospace Medicine*. Available from: <http://www.avmed.in/2012/06/protection-against-the-g/> [Accessed: Oct 1, 2017]
- [36] Wood E. Development of anti-G suits and their limitations. *Aviation, Space, and Environmental Medicine*. 1987;**58**(7):699-706
- [37] Wood E, Code C, Baldes E. Partial supination versus Gz protection. *Aviation, Space, and Environmental Medicine*. 1990;**61**(9):850-858
- [38] Burns J, Ivan D, Stern C, Patterson J, Johnson P, Drew W, et al. Protection to +12 Gz. *Aviation, Space, and Environmental Medicine*. 2001;**72**(5):413-421

- [39] Albery W. Acceleration in other axes affects +Gz tolerance: Dynamic centrifuge simulation of agile flight. *Aviation, Space, and Environmental Medicine*. 2004;**75**(1):1-6
- [40] Tacker W Jr, Balldin U, Burton R, Glaister D, Gillingham K, Mercer J. Induction and prevention of acceleration atelectasis. *Aviation, Space, and Environmental Medicine*. 1987;**58**(1):69-75
- [41] O'Brien J. Absorption atelectasis: Incidence and clinical implications. *American Association of Nurse Anesthetists*. 2013;**81**(3):205
- [42] Haswell M, Tacker W Jr, Balldin U, Burton R. Influence of inspired oxygen concentration on acceleration atelectasis. *Aviation, Space, and Environmental Medicine*. 1986;**57**(5):432-437
- [43] Lange B, Torp-Svendsen J, Toft P. Neck pain among fighter pilots after the introduction of the JHMCS helmet and NVG in their environment. *Aviation, Space, and Environmental Medicine*. 2011;**82**(5):559-563
- [44] Shiri R, Frilander H, Sainio M, Karvala K, Sovellius R, Vehmas T, et al. Cervical and lumbar pain and radiological degeneration among fighter pilots: A systematic review and meta-analysis. *Occupational and Environmental Medicine*. 2015;**72**(2):145-150. DOI: 10.1136/oemed-2014-102268
- [45] De Loose V, Van den Oord M, Burnotte F, Van Tiggelen D, Stevens V, Cagnie B, et al. Individual, work, and flight-related issues in F-16 pilots reporting neck pain. *Aviation, Space, and Environmental Medicine*. 2008;**79**(8):779-783
- [46] Verde P, Trivelloni P, Angelino G, Morgagni F, Tomao E. Neck pain in F-16 vs. typhoon fighter pilots. *Aerospace Medicine and Human Performance*. 2015;**86**(4):402-406. DOI: 10.3357/AMHP.4063.2015
- [47] Chumbley E, O'Hair N, Stolfi A, Lienesch C, McEachen J, Wright B. Home cervical traction to reduce neck pain in fighter pilots. *Aerospace Medicine and Human Performance*. 2016;**87**(12):1010-1015. DOI: 10.3357/AMHP.4625.2016
- [48] Four Ways Upgraded Ejection Seat Modifications Can Keep Our Pilots Safe [Internet]. *The Washington Post*. 2009. Available from: <http://www.washingtonpost.com/sf/brand-connect/wp/enterprise/four-ways-upgraded-ejection-seat-modifications-can-keep-our-pilots-safe/> [Accessed: Oct 1, 2017]
- [49] Ejection Seat Market Is Changing Pace [Internet]. 2017. Available from: <http://aviationweek.com/air-combat-safety/ejection-seat-market-changing-pace> [Accessed: Oct 12, 2017]
- [50] Collins R, McCarthy G, Kaleps I, Knox F. Review of major injuries and fatalities in USAF ejections, 1981-1995. *Biomedical Sciences Instrumentation*. 1997;**33**:350-353
- [51] Kang K-W, Shin YH, Kang S. Acute spinal injury after centrifuge training in asymptomatic fighter pilots. *Aerospace Medicine and Human Performance*. 2015;**86**(4):386-391. DOI: 10.3357/AMHP.4062.2015

- [52] Puderbaugh M. A report of transverse process fractures secondary to the centrifuge in a healthy aviator. *Aerospace Medicine and Human Performance*. 2016;**87**(7):655-658. DOI: 10.3357/AMHP.4541.2016
- [53] Kikukawa A, Tachibana S, Yagura S. G-related musculoskeletal spine symptoms in Japan Air Self Defense Force F-15 pilots. *Aviation, Space, and Environmental Medicine*. 1995;**66**(3):269-272
- [54] Lindgren T, Wieslander G, Dammström B, Norbäck D. Tinnitus among airline pilots: Prevalence and effects of age, flight experience, and other noise. *Aviation, Space, and Environmental Medicine*. 2009;**80**(2):112-116
- [55] Elmenhorst E, Elmenhorst D, Wenzel J, Quehl J, Mueller U, Maass H, et al. Effects of nocturnal aircraft noise on cognitive performance in the following morning: Dose-response relationships in laboratory and field. *International Archives of Occupational and Environmental Health*. 2010;**83**(7):743-751. DOI: 10.1007/s00420-010-0515-5
- [56] Rhee M, Kim H, Roh S, Kim H, Kwon H. The effects of chronic exposure to aircraft noise on the prevalence of hypertension. *Hypertension Research*. 2008;**31**(4):641-647. DOI: 10.1291/hypres.31.641
- [57] Rajguru R. Military aircrew and noise-induced hearing loss: Prevention and management. *Aviation, Space, and Environmental Medicine*. 2013;**84**(12):1268-1276
- [58] Department of Defense Office F-JP. F-35 Noise Measurement Executive Summary. [Internet] 2014. Available from: http://www.jsf.mil/news/docs/20141031_F-35_Noise_Executive_Summary.pdf [Accessed: Oct 13, 2017]
- [59] Newman E. Speech and hearing. In: Gray D, editor. *American Institute of Physics Handbook*. 3rd ed. New York: McGraw-Hill Book Co., Inc; 1957. pp. 3-155
- [60] Harris C, Shoenberger R. Combined effects of broadband noise and complex waveform vibration on cognitive performance. *Aviation, Space, and Environmental Medicine*. 1980;**51**(1):1-5
- [61] Griffin M. A comparison of standardized methods for predicting the hazards of whole-body vibration and repeated shocks. *Journal of Sound and Vibration*. 1998;**215**(4):883-914
- [62] El Falou W, Duchêne J, Grabisch M, Hewson D, Langeron Y, Lino F. Evaluation of driver discomfort during long-duration car driving. *Applied Ergonomics*. 2003;**34**(3):249-255
- [63] Smith S. Characterizing the effects of airborne vibration on human body vibration response. *Aviation, Space, and Environmental Medicine*. 2002;**73**(1):36-45
- [64] Bongers P, Hulshof C, Dijkstra L, Boshuizen H, Groenhout H, Valken E. Back pain and exposure to whole body vibration in helicopter pilots. *Ergonomics*. 1990;**33**(8):1007-1026
- [65] Gaydos S. Low back pain: Considerations for rotary-wing aircrew. *Aviation, Space, and Environmental Medicine*. 2012;**83**(9):879-889
- [66] Orlady W, Orlady M. *Human Factors in Multi-Crew Flight Operations*. Aldershot, England: Ashgate; 1999

- [67] Door R. *Air Combat: A History of Fighter Pilots*. New York, NY: The Berkley Publishing Group; 2006
- [68] Shetty J, Lawson C, Shahneh A. Simulation for temperature control of a military aircraft cockpit to avoid pilot's thermal stress. *CEAS Aeronautical Journal*. 2015;**6**(2):319-333
- [69] Robinson TSgt 1st MXG/MXQ. Department of Defense Langley Air Force Base Briefing: F-22 03-041 Stuck Canopy [Internet]. 2006. Available from: <http://www.spaceref.com/news/viewsr.html?pid=20396> [Accessed: Oct 1, 2017]
- [70] Nunneley S, Flick C. Heat stress in the A-10 cockpit: Flights over desert. *Aviation, Space, and Environmental Medicine*. 1981;**52**(9):513-516
- [71] Lee A. *Open Cockpit*. London, UK: Grub Street; 2012
- [72] Centers for Disease Control and Prevention Criteria for a Recommended Standard: Occupational Exposure to 1,1,2,2-Tetrachloroethane [Internet]. 1976. The National Institute for Occupational Safety and Health. Available from: <https://www.cdc.gov/niosh/nioshtic-2/00068146.html> [Accessed: Oct 1, 2017]
- [73] Heffter K. Industrial poisoning by tetrachloroethane. *Vierteljahresschr Gerichtl Med Oeff Sanitaetswes*. 1914;**48**:109-114
- [74] Willcox W, Spilsbury B, Legge T. An outbreak of toxic jaundice of a new type amongst aeroplane workers—Its clinical and toxicological aspect. *Transactions of the Medical Society of London*. 1915;**38**:129-156
- [75] Browning E. *Toxicity and Metabolism of Industrial Solvents*. 1st ed. New York: Elsevier; 1965
- [76] Harrison V, RS M. An emerging concern: Toxic fumes in airplane cabins. *Cortex*. 2016;**74**: 297-302. DOI: 10.1016/j.cortex.2015.11.014
- [77] Nicholas J, Butler G, Lackland D, Tessier G, Mohr L Jr, Hoel D. Health among commercial airline pilots. *Aviation, Space, and Environmental Medicine*. 2001;**72**(9):821-826
- [78] Bagshaw M. Health Effects of Contaminants in Aircraft Cabin Air: Summary Report v2.7. [Internet]. 2014. Available from: <https://www.asma.org/asma/media/asma/Travel-Publications/Air-contamination-health-effects-report-v2-7-Apr2014.pdf> [Accessed: Oct 1, 2017]
- [79] Hussain S, Frazier J. Cellular toxicity of hydrazine in primary rat hepatocytes. *Toxicological Sciences*. 2002;**69**(2):424-432
- [80] Latendresse J, Marit G, Vernot E, Haun C, Flemming C. Oncogenic potential of inhaled hydrazine in the nose of rats and hamsters after 1 or 10 1-hr exposures. *Toxicological Sciences*. 1995;**27**(1):33-48
- [81] National Institute for Occupational Safety and Health Guideline for Hydrazine: Potential Human Carcinogen [Internet]. 1988. Available from: <https://www.cdc.gov/niosh/docs/81-123/pdfs/0329.pdf> [Accessed: Oct 1, 2017]

- [82] Christensen W. Industrial hygiene and the F-16 air combat fighter. *Aviation, Space, and Environmental Medicine*. 1981;**52**(3):147-149
- [83] Sanlorenzo M, Wehner M, Linos E, Kornak J, Kainz W, Posch C, et al. The risk of melanoma in airline pilots and cabin crew: A meta-analysis. *JAMA Dermatology*. 2015; **151**(1):51-58. DOI: 10.1001/jamadermatol.2014.1077
- [84] Cadilhac P, Bouton M, Cantegril M, Cardines C, Gisquet A, Kaufman N, et al. In-flight ultraviolet radiation on commercial airplanes. *Aerospace Medicine and Human Performance*. 2017;**88**(10):947-951. DOI: 10.3357/AMHP.4852.2017
- [85] Band P, Spinelli J, Ng V, Moody J, Gallagher R. Mortality and cancer incidence in a cohort of commercial airline pilots. *Aviation, Space, and Environmental Medicine*. 1990;**61**(4): 299-302
- [86] Di Trollo R, Di Lorenzo G, Fumo B, Ascierio P. Cosmic radiation and cancer: Is there a link? *Future Oncology*. 2015;**11**(7):1123-1135. DOI: 10.2217/fon.15.29
- [87] Raslau D, Dabrh A, Moain A, Summerfield D, Wang Z, Steinkraus L, et al. Prostate cancer in pilots. *Aerospace Medicine and Human Performance*. 2016;**87**(6):565-570. DOI: 10.3357/AMHP.4453.2016
- [88] Ernsting J. The ideal relationship between inspired oxygen concentration and cabin altitude. *Aerospace Medicine*. 1963;**34**:991
- [89] United States Airforce Scientific Advisory Board: Aircraft Oxygen Generation SAB-TR-11-04 [Internet]. 2012. Available from: http://www.airforcemag.com/DocumentFile/Documents/2012/AFSAB_Oxygen_020112.pdf [Accessed: Oct 1, 2017]
- [90] Bumiller E. Oxygen Problems on F-22 Elude the Air Force's Fixes. *The New York Times*. July 2, 2012
- [91] Ferran L. F-22 Raptor, America's Most Expensive Fighter, Grounded Again After Oxygen Scare [Internet]. 2011. Available from: <http://abcnews.go.com/Blotter/22-raptor-grounded-oxygen-scare/story?id=14802706> [Accessed: Oct 1, 2017]
- [92] Fox News. US Navy grounds T-45 training fleet following Fox News Report [Internet]. 2017. Available from: <http://www.foxnews.com/politics/2017/04/05/us-navy-grounds-t-45-training-jet-fleet-following-fox-news-report.html> [Accessed: Oct 1, 2017]
- [93] CNN. F-35 fighters grounded indefinitely over oxygen issues [Internet]. 2017. Available from: <http://www.cnn.com/2017/06/12/politics/f-35-grounded-indefinitely-oxygen-problems/index.html> [Accessed: Oct 1, 2017]
- [94] West J. A strategy for in-flight measurements of physiology of pilots of high-performance fighter aircraft. *Journal of Applied Physiology*. 2013;**115**(1):145-149. DOI: 10.1152/japplphysiol.00094.2013
- [95] Flottman LCJ. Acceleration Atelectasis in the F-22 [Internet]. 2013. Chicago, IL: Aerospace Medicine Conference. Available from: http://asmameeting.org/asma2013_mp/pdfs/asma2013_present_510.pdf [Accessed: Oct 1, 2017]

- [96] McEachen J, Issa A, Marck J, Steinkraus L, Johnson B. Real-time effects of normobaric, transient near-anoxia on performance. *Aerospace Medicine and Human Performance*. 2015;**86**(2):76-81. DOI: 10.3357/AMHP.4041.2015
- [97] Hosseini S, Bruno J, Baker J, Gundran A, Harbott L, Gerdes J, et al. Neural, physiological, and behavioral correlates of visuomotor cognitive load. *Scientific Reports*. 2017;**7**(1): e8866. DOI: 10.1038/s41598-017-07897-z
- [98] Alnæs D, Sneve M, Espeseth T, Endestad T, van de Pavert S, Laeng B. Pupil size signals mental effort deployed during multiple object tracking and predicts brain activity in the dorsal attention network and the locus coeruleus. *Journal of Vision*. 2014;**14**(4):1-1
- [99] Stepanek J, Pradhan G, Cocco D, Smith B, Bartlett J, Studer M, et al. Acute hypoxic hypoxia and isocapnic hypoxia effects on oculometric features. *Aviation, Space, and Environmental Medicine*. 2014;**85**(7):700-707
- [100] Van Liere E, Stickney J. *Hypoxia*. Chicago and London: The University of Chicago Press; 1963
- [101] Marshall S. Identifying cognitive state from eye metrics. *Aviation, Space, and Environmental Medicine*. 2007;**78**(5):B165-B175
- [102] Albery W. Multisensory cueing for enhancing orientation information during flight. *Aviation, Space, and Environmental Medicine*. 2007;**78**(5):B186-B190
- [103] Thomas M, Russo M. Neurocognitive monitors: Toward the prevention of cognitive performance decrements and catastrophic failures in the operational environment. *Aviation, Space, and Environmental Medicine*. 2007;**78**(5):B144-B152
- [104] Tsai Y, Viirre E, Strychacz C, Chase B, Jung T. Task performance and eye activity: Predicting behavior relating to cognitive workload. *Aviation, Space, and Environmental Medicine*. 2007;**78**(5):B176-B185
- [105] Connolly D. Spatial contrast sensitivity at twilight: Luminance, monocularly, and oxygenation. *Aviation, Space, and Environmental Medicine*. 2010;**81**(5):475-483
- [106] Ernst G. Heart-rate variability – More than heart beats? *Frontiers in Public Health*. 2017; **5**:240. DOI: 10.3389/fpubh.2017.00240
- [107] Auto-GCAS Saves Unconscious F-16 Pilot-Declassified USAF Footage [Internet]. 2016. *Aviation Week & Space Technology*. Available from: <http://aviationweek.com/air-combat-safety/auto-gcas-saves-unconscious-f-16-pilot-declassified-usaf-footage> [Accessed: Oct 2, 2017]
- [108] Chait R, Lyons J, Long D. Critical Technology Events in the Development of the Apache Helicopter: Project *Hindsight* Revisited. Washington, DC: Center for Technology and National Security Policy; 2006. 27 p
- [109] Cognitive Avionics Toll Set (CATS) Software [Internet]. Available from: <https://hfddata.opl.uiowa.edu/opl/?q=cats> [Accessed: Oct 1, 2017]
- [110] BBC News. Ministry of Defence to sell 13 sites for 17,000 homes [Internet]. 2016. Available from: <http://www.bbc.com/news/uk-37287613> [Accessed: Oct 23, 2017]