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This journal, representing the members of the Aerospace Medical Association, is published for those interested in aerospace medicine and human performance. It is devoted to serving and supporting all who explore, travel, work, or live in hazardous environments ranging from beneath the sea to the outermost reaches of space.

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ADVANCE REGISTRATION FORM
AEROSPACE MEDICAL ASSOCIATION
94th ANNUAL SCIENTIFIC MEETING

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(See reverse for workshops & events)

*****NOTE: WORKSHOPS ARE LIMITED *** REGISTER EARLY*****

WORKSHOP DATE/NAME		FEE	Total Fee
☐Sun., May 5, 8:00 am – 5:00 am Workshop: "Aerospace Epidemiology – The Science of the Denominator" (MAX 50)		$200	
☐Sun., May 5, 8:00 am – 5:00 pm Workshop: "Clear Skies Ahead: Achieving and Sustaining Mental Wellness in the Aerospace System of Tomorrow" (MAX 125)		$200	
☐Sun., May 5, 9:00 am – 4:00 pm Workshop: "Understanding and Managing Fatigue in Aviation" (MAX 75)		$150	
☐Fri., May 10, 8:00 am – 5:00 pm Workshop: "Space Mission Analogs: Medical Care in Remote Maritime Operations" (MAX 30)		$250	
EVENTS *(NOTE: Advance Purchase Only requires tickets to be purchased during Early Bird & Advance Registration – no tickets for these events will be sold onsite)*	**# OF TICKETS**	**FEE PER TICKET**	**TOTAL FEE**
☐Sun., May 5, AsMA Welcome to Chicago **(NOTE: All Attending Event Must Have Tickets)**		$15	
☐Mon., May 6, 6:00 am, Richard B. "Dick" Trumbo 5K Fun Run/Walk ***(Advance Purchase Only)***		$15	
☐Mon., May 6, American Society of Aerospace Medicine Specialists (ASAMS) Breakfast & Business Meeting ***(Advance Purchase Only)*** **(ASAMS Members Only)**		$25	
☐Mon., May 6, Aerospace Human Factors Association Luncheon ***(Advance Purchase Only)***		$50	
☐Mon., May 6, Civil Aviation Medical Association Luncheon ***(Advance Purchase Only)***		$50	
☐Mon., May 6, Society of U.S. Air Force Flight Surgeons Luncheon ***(Advance Purchase Only)***		$50	
☐Mon., May 6, Society of U.S. Army Flight Surgeons Luncheon ***(Advance Purchase Only)***		$50	
☐Mon., May 6, U.S. Navy Luncheon ***(Advance Purchase Only)***		$50	
☐Mon., May 6, Fellows Dinner ***(Advance Purchase Only)*** **(MUST BE A FELLOW OR GUEST OF AsMA FELLOW)**		$90	
☐Tues., May 7, Associate Fellows Breakfast ***(Advance Purchase Only)***		$50	
☐Tues., May 7, AsMA Annual Business Meeting ***(Advance Purchase Only)*** **(Free Attendance; Ticket required for meal)**		$50	
☐Tues., May 7, Alliance of Air National Guard Flight Surgeons Luncheon ***(Advance Purchase Only)***		$50	
☐Tues., May 7, Reception to Honor International Attendees		$25	
☐Wed., May 8, Canadian Society of Aerospace Medicine Breakfast ***(Advance Purchase Only)***		$50	
☐Wed., May 8, Aerospace Nursing & Allied Health Professionals Society Luncheon ***(Advance Purchase Only)***		$50	
☐Wed., May 8, Aerospace Physiology Society Luncheon ***(Advance Purchase Only)***		$50	
☐Wed., May 8, Iberoamerican Association of Aerospace Medicine Luncheon ***(Advance Purchase Only)***		$50	
☐Wed., May 8, Society of NASA Flight Surgeons Luncheon ***(Advance Purchase Only)***		$50	
☐Thur., May 9, Space Medicine Association Luncheon		$50	
☐Thur., May 9, AsMA Honors Night Banquet **(Black Tie Optional)**		$90	
		SUBTOTAL OF EVENTS	
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May 5 - 9, 2024
Hyatt Regency, Chicago
Chicago, Illinois

The WING of AsMA
AsMA 94th Annual Scientific Meeting

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Please read the entire form before filling out or registering online. Fill out a separate form for each registrant.
Advance Registration closes *April 19, 2024*. No refunds *after April 26, 2024.*
Enter the TOTAL NUMBER of tickets and TOTAL DOLLAR AMOUNT on the line after each activity.
Send your advance registration directly to THE WING or register online.
DO NOT include with your spouse's/sponsor's AsMA registration.

***PLEASE NOTE: All prices are in U.S. dollars. Only U.S. funds will be accepted for Registration.**

NOTE: Registration is mandatory for participation in Wing activities.

Wing Dues (May 2024 – May 2025) **$35.00** $________________
☐ New Member 2024 ☐ Renewal ☐ 2024 Dues Previously Paid

Compulsory Registration Fee (advanced reg. $40.00, on-site: $50.00) $________________

- **Monday, May 6, Welcome Reception, 1:00 PM – 4:30 PM**
  The WING Welcome Reception for Registrants only **INCLUDED** No.____ $ 0.00
- **Tuesday, May 7, 10:00 AM – 12:00 PM** **$45.00** No.____ $___________
  (Meet in Lobby @ 9:30 AM)
  Architectural Boat Tour
- **Wednesday, May 8, 11:00 AM – 1:00 PM** **$50.00** No.____ $__________
  (Meet in Lobby @ 10:30 AM)
  Annual Wing Luncheon & Business Meeting McCormick & Schmick's
- **Thursday, May 9, All Day!** **$0.00**
  Chicago at your Leisure. You pick where and with whom and go!

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The Wing of AsMA
Annual Meeting and Tour Information

WELCOME RECEPTION

Monday, May 6, 1:30-4:30 PM

Connect with old friends and make some new ones in a relaxed environment at our annual Welcome Reception. *Remember to bring a small gift reminiscent of your home city, state or country for the gift exchange and please include a short note letting the recipient know who/where the gift is from.* ***New members and first-time attendees don't bring a gift as we are very happy to welcome you to THE WING!***

This year's Welcome Reception will be held in **THE Hyatt Regency CHICAGO HOTEL, *Plaza Ballroom A.***

Architectural Boat Tour

Tuesday, May 7, 10:00 AM – 12:00 PM $45.00

Meet at 9:30 AM in the Lobby at The Hyatt Regency Chicago Hotel.

Tips included. After return to the hotel, lunch is on your own.

Discover the architectural gems of the Windy City from an ideal vantage point on a cruise down the Chicago River. Covering more than 130 years of architectural history, the tour is the perfect opportunity to see a huge area of the city. Enjoy unobstructed views of the city's top attractions and gain an in-depth understanding of local architecture.

ANNUAL WING LUNCHEON & BUSINESS MEETING $50.00

McCormick's & Schmick's

Wednesday, May 8, 11:00 AM – 1:00 PM

1 East Wacker Drive, Chicago IL.

Meet in the lobby at 10:30 AM. We can walk together (a short walk from the hotel). We'll enjoy a lovely meal, discuss a little business and catch up with friends. Our Annual Wing Business meeting will be held in a delightful setting on East Wacker Street. Of course, it's just minutes away from the Chicago Theater, Oriental Theater, Millennium Park, various fun and unique Chicago shops. Please email to: **asmawing@gmail.com** if you request one of the dietary alternatives by **April 19, 2024.**

Thursday, May 9, All Day

Meet up with friends to head out for your favorite adventure. There is more to do in Chicago than pretty much anywhere else we've been! The weather should be great so bring some good walking shoes. Whether it's shopping on the Magnificent Mile, seeking adventure at the Navy Pier, relaxing at Millennial Park or touring the Chicago museums, it is all your choice. You cannot go wrong.

AsMA and UHMS … from Sea to Air to Space

Joseph Dervay, M.D., M.P.H., MMS, FACEP, FAsMA, FUHM

As a longtime member of both the Aerospace Medical Association (AsMA) and the Undersea & Hyperbaric Medical Society (UHMS), I have always enjoyed the challenges of human physiology and medicine across the "pressure spectrum from sea to air to space". This includes the scope of preventive medicine and human performance aspects of caring for individuals working in those environments.

AsMA and UHMS have organizational paths that have intertwined over the decades. I wish to share with you an initiative the leadership of AsMA and UHMS have been thoughtfully, and methodically, examining regarding potential future interactions between these professional organizations.

The *Undersea Medical Society* (UMS) was initially formed in 1967 as a Constituent group of AsMA by a cadre primarily of U.S. Navy undersea medical physicians. Over time UMS expanded to include additional members who were not necessarily part of the aeromedical community and, subsequently, left AsMA to become an independent organization in 1974. With the ongoing advancement of clinical hyperbaric medicine in the 1970s and 1980s, UMS continued to grow and was renamed the *Undersea and Hyperbaric Medical Society* (UHMS) in 1986. A number of AsMA members have historically belonged to both organizations.

In 1998, AsMA and UHMS held a Joint Annual Scientific Meeting in Seattle which was truly a wonderful opportunity to engage in professional exchange. It was not until 2022 that AsMA and UHMS again combined forces for a Joint Annual Scientific Meeting upon the encouragement of members crossing both communities. Most meeting attendees in Reno *were not even trained or working 24 years prior* when the organizations met, so it was incumbent upon the Scientific Program Committee to develop program tracks specific to each organization's interests as well as areas of common interest. The program included a number of panels and sessions pertinent to members of both groups, such as extravehicular activities (EVA), new generation spacesuits, exploration atmospheres, decompression sickness and treatment, and a variety of other barophysiology topics. The Tuesday morning Reinartz Panel was entitled, "Overcoming Barriers on the Pressure Spectrum: From the Past to the Future." I was honored to host an outstanding panel with expertise across the barophysiology arena. The format consisted of brief formal presentations by panelists and a moderated discussion, and included; Dr. Jay Dean (Physiological barriers encountered in WWII aviation that drove advancements in decompression physiology and oxygen toxicity); Dr. Richard Moon (Physiological barriers of deep-sea commercial diving using data about oxygen toxicity and decompression to break depth records); Dr. Jonathan Clark (Physiological barriers of high-altitude parachute operations required solutions informed by both diving and aviation), and former NASA Astronaut Dr. Michael Gernhardt (Knowledge from diving decompression drove solutions for astronaut EVA protocols, and commercial diving technology led to innovations for working in microgravity).

The feedback received throughout the 2022 Annual Meeting and through post-meeting surveys was truly excellent and very complimentary of the combined meeting approach. A strong desire to establish further such meetings was conveyed. Subsequently, both organizations decided to hold the next Joint meeting in Atlanta in 2025, with a further decision by AsMA and UHMS to schedule combined meetings for the foreseeable future after 2025. What a wonderful opportunity for members of both organizations to share science, knowledge, and establish collegial connections.

As directed by the AsMA Executive Committee, our Executive Director (ED) Jeff Sventek has been actively engaging with the UHMS ED John Peters to address various aspects of enhanced collaboration and integration. Of note, both AsMA and UHMS are international non-profit organizations, maintain membership levels over 2000, and are similar in their financial profiles. The organizations currently have a shared services agreement whereby UHMS delivers CME accreditation and electronic poster capability to AsMA. The November 2023 AsMA Council was supportive of exploring further cooperation.

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CONTACT DETAILS:
Email: President@asma.org • **Web site:** www.asma.org • **Facebook:** Aerospace Medical Association • **Twitter:** @Aero_Med

PRESIDENT'S PAGE, *continued*

The February 2024 Executive Committee meeting held in Texas included an additional day entirely dedicated to an AsMA/UHMS Collaboration Meeting, which included the in-person participation of UHMS ED John Peters and President-Elect Dr. Owen O'Neill. The agenda included exploring issues such as combined services, operations, governance, policies and procedures, and joint membership. *Careful thought and consideration were given to identifying and maintaining the cultural and historic aspects of each organization.* Possible future interactions range the spectrum from expanded shared services, creation of a formal Alliance to share staff and other resources, to further levels of integration. A formal debrief and recommendations resulting from the Executive Committee discussions in February will be presented at the May Council meeting and in future correspondences.

During Astronaut-Physician Kjell Lindgren's greeting, sent from the International Space Station, at the beginning of the 2022 Reinartz Panel (discussed above), he stated to the audience, "Thank you for your incredible dedication to the health, safety, and performance of all humans that operate in the aviation, space, undersea, and hyperbaric environments. Without your professional expertise, I would not be speaking to you today from the International Space Station."

Dr. Lindgren's comments reinforced what colleagues holding membership in both AsMA and UHMS have known all along … that we are indeed complementary professional organizations, with a historical connection, and with much overlap of scientific knowledge and technical challenges.

We are optimistically, yet cautiously and thoughtfully, keeping an open-minded approach to see where future collaboration may lead us!

Keep 'em Flying…and Full Steam Ahead.

Physiological Fitness of U.S. Army Aviators Compared to the U.S. General Population

Matthew D'Alessandro; Ryan Mackie; Samantha Wolf; James S. McGhee; Ian Curry

INTRODUCTION: U.S. Army aviators are required to maintain a level of physiological fitness as part of their qualifying process, which suggests that they are generally physically healthy. However, it has not been statistically proven that they are more "physiologically fit" than the general population.

METHODS: This retrospective study compares physiological measurements of U.S. Army aviators from the Aeromedical Electronic Resource Office database to the U.S. general population using the Center for Disease Control's National Health and Nutrition Examination Survey data. To enable an accurate comparison of physiological metrics between U.S. Army aviators and the U.S. general population, aviators were categorized into the same age groups and biological genders used for segmentation of the national population data.

RESULTS: On average, pulse rate was 4.85 bpm lower in male aviators and 6.84 bpm lower in female aviators. Fasting glucose levels were, on average, 10.6 mg · dL^{-1} lower in aviators compared to the general population. Key metrics like pulse rate and fasting glucose were lower in aviators, indicating cardiovascular and metabolic advantages. However, parameters like cholesterol showed less consistent differences.

DISCUSSION: While aviation physical demands and administrative policies selecting for elite physiological metrics produce improvements on some dimensions, a nuanced view accounting for the multitude of factors influencing an aviator's physiological fitness is still warranted. Implementing targeted health monitoring and maintenance programs based on assessments conducted more frequently than the current annual flight physical may optimize aviator safety and performance over the course of a career.

KEYWORDS: aviator, physiological fitness, Aeromedical Policy Letters.

D'Alessandro M, Mackie R, Wolf S, McGhee JS, Curry I. *Physiological fitness of U.S. Army aviators compared to the U.S. general population*. Aerosp Med Hum Perform. 2024; 95(4):175–186.

While all U.S. soldiers must meet basic standards of physical fitness as outlined in U.S. Army Regulation 40-501, U.S. Army aviators are held to more stringent physical and mental requirements due to the unique demands of aviation duties. Specifically, Chapter 4 of the regulation and supporting Aeromedical Policy Letters outline elevated standards for visual acuity, color vision, depth perception, and other physiological metrics critical for in-flight performance and safety.[24] These metrics can also aid in identifying U.S. soldiers who are at risk for injuries and the development of health problems.[11,15] Though a wide range of individual variability exists between aviators, aviation standards and Aeromedical Policy Letters are precise given the immense risks inherent to flight.[6,20] Ultimately, the aviation branch depends on these standards to mitigate dangers and ensure only qualified U.S. soldiers operate Army aircraft. Although physical and mental fitness standards apply to all U.S. soldiers, the demands placed specifically on U.S. Army aviators within the aviation domain necessitate more specialized physical and cognitive capabilities that distinguish this population from the broader military community.

Monitoring physiological metrics makes it possible, in some cases, to identify U.S. soldiers at risk for developing health

From the U.S. Army Aeromedical Research Laboratory and the Oak Ridge Institute for Science and Education, Fort Novosel, AL, United States.

This manuscript was received for review in September 2023. It was accepted for publication in January 2024.

Address correspondence to: Matthew D'Alessandro, Ph.D., 6901 Farell Dr., Fort Novosel, AL 36362, United States; matthew.g.dalessandro2.mil@health.mil.

DOI: https://doi.org/10.3357/AMHP.6371.2024

problems and enables healthcare providers to take steps to prevent these problems.[5] In addition to their high level of physical fitness, aviators experience environmental stressors that have a substantial effect on their physiology compared to other military professions. The flight environment exposes aviators to stressors associated with dynamic aircraft, such as gravitational forces, noise, vibration, alterations in barometric pressure, and temperature variation.[23] In addition to supplemental stressors aviators experience due to the dynamic environment, several genetic and gender-specific variables directly affect physiology.[18] As flight physiology is a critical aspect of aviation safety, it is essential to understand the physiological status of aviators to ensure safe and efficient operations.[3]

Although it has been assumed that aviators are more "physiologically fit" than the general population, to our knowledge, this assumption has not been statistically proven. It is important to quantify the difference in physiological fitness between U.S. Army aviators and the U.S. general population to inform aeromedical policy and standards. For this study, we differentiate physiological fitness (e.g., cardiovascular endurance, muscle strength, etc.) from physical fitness more broadly. We compared specific physiological measurements of U.S. Army aviators obtained from the Aeromedical Electronic Resource Office (AERO) database to values of individuals indexed in the U.S. Center for Disease Control and Prevention's National Health and Nutrition Examination Survey (CDC NHANES) database for the years 2012–2018. The CDC NHANES data represent the U.S. general population. We grouped aviators and the general population into biological gender and age-grouped categories to allow for statistical comparisons to assess if the U.S. aviation population is significantly "more physiologically fit" than the U.S. general population.

METHODS

Subjects

Prior to data acquisition and analysis, the study was reviewed and approved according to the U.S. Army Aeromedical Research Laboratory's Human Subjects Research Protection Plan. The USAARL Determination Official determined that the study met the criteria for exemption from Institutional Review Board review. The present study is retrospective in design, using de-identified data from the AERO medical record system (January 2013–December 2018) and publicly available data from the CDC NHANES database.

Procedure

AERO is a database system the U.S. Army, U.S. Navy, and U.S. Coast Guard use to record flight physical examinations for aviators, crewmembers, and aviation students. The anonymized dataset from AERO for this study contains information on all U.S. Army aviation personnel who received a Class II flight physical [rated aviator initial physical and rated aviator comprehensive (comprehensive every year (long) and interval (short)]. The dataset provided to the researchers contains the demographic variables of age and gender, but otherwise does not contain personally identifiable information. U.S Army aviators are required to complete a flight physical at least once every year. Aviators may also have multiple AERO entries within 1 yr due to follow-up assessments. To match the structure of the CDC NHANES 2-yr collection cycles, the AERO data were averaged into a single data entry for each unique aviator for each 2-yr window.

CDC NHANES is a program of surveys and studies conducted by the Centers for Disease Control and Prevention to assess the health and nutritional status of adults and children in the United States.[16] The CDC NHANES dataset is organized as a stratified, multistage probability sample. However, for this study, we treated the CDC NHANES data as a random sample of the U.S. population to allow for comparison with the AERO dataset. The final data used for statistical analysis contains 24,259 observations from AERO and 12,001 observations from CDC NHANES covering the years 2013–2018. Each observation from AERO represents one flight physical for a given 2-yr period. Each observation from CDC NHANES represents a unique individual for a given 2-yr period. The outcome variables of interest in both data sets are pulse, systolic and diastolic blood pressure, hematocrit, hemoglobin, fasting blood sugar, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides. Individuals with missing or extreme medical values were not included in the analysis.

Statistical Analysis

Descriptive statistics and plotting were performed using R (v4.2.1; R Core Team, Vienna, Austria; 2022), R Studio (2022.12.0 Build 353), and tidyverse (v2.0.0). Statistical analyses were performed using R (v4.2.1; R Core Team, 2022), tidyverse,[25] rstatix,[8] and WRS2 packages.[9] The purpose of the descriptive statistics performed in this study was simply to assess any potential statistical significance between groups. Therefore, inferential statistics were only used to support the observable data trends. The significance testing criterion was set at $P = 0.05$. To maintain appropriate statistical power and reduce the chance of a Type 1 error, the data was reduced to 150 observations per group before inferential testing (group is defined as each unique combination of age and flight status). Two-way analyses of variance (ANOVAs) were used to estimate the effect of age (four levels: 16–25, 26–35, 36–45, and 46–55), flight status (two levels: AERO and CDC NHANES), and the interaction effect for each outcome variable in the data. The assumptions of the two-way ANOVA were tested using the Shapiro-Wilk test (for normality of residuals) and Levene's test (for homogeneity of variance). When the assumptions for the two-way ANOVA were violated, a robust two-way ANOVA with 20% trimmed means was used (WRS2 package). When the interaction effect was significant, one-way ANOVAs were used to determine the effect of flight status for each age group. When the effect of age was significant, pairwise comparisons were made using *t*-tests (or the robust equivalent as described in the WRS2 documentation). *P*-values for one-way ANOVAs and pairwise comparisons were adjusted using the Bonferroni method. Importantly, *P*-values only pertain to the random samples used; however, the figures and summary statistics include all available data.

RESULTS

Our retrospective study compared the physiological metrics of U.S. Army aviators to those of the U.S. general population. We grouped the U.S. Army aviators and the U.S. general population by age and biological gender. The results of this study are represented in **Fig. 1, Fig. 2, Fig. 3, and Fig. 4** and **Table I**. A total of 24,259 U.S. Army aviators from the AERO database and 12,001 individuals from the CDC NHANES database were included in the analysis. Comparisons were made between U.S. Army aviators and the U.S. general population across age groups and biological sex for several physiological metrics.

U.S. Army male aviators demonstrated significantly lower pulse rates compared to the U.S. general population [$F(1, 1192) = 48.95$, $P < 0.001$]. U.S. Army female aviators showed a significant interaction effect between age and flight status [$F(3, 1150) = 12.18$, $P = 0.008$]. Pairwise comparisons showed that aviators had significantly lower pulse rates across all age groups ($P \leq 0.021$ for all). U.S. Army male aviators showed a significant interaction effect for diastolic blood pressure (BP) [$F(3, 1192) = 25.17$, $P < 0.001$] and systolic BP [$F(3, 1192) = 26.90$, $P < 0.001$]. Pairwise comparisons showed that U.S. Army male aviators had significantly higher diastolic and systolic BP compared to the U.S. general population in the youngest two age groups ($P < 0.01$ for all). U.S. Army female aviators also had a significant interaction effect for diastolic BP [$F(3, 1150) = 17.78$, $P < 0.001$] and systolic BP [$F(3, 1148) = 35.06$, $P < 0.001$]. Pairwise comparisons showed that U.S. Army female aviators had significantly higher diastolic and systolic BP compared to the U.S. general population in the youngest two age groups ($P < 0.01$ for all). Additionally, U.S Army female aviators in the 46–55 age group showed a significantly lower systolic BP than the U.S. general population ($P = 0.012$). Interestingly, the interaction plots show that aviator blood pressure for both men and women stay relatively consistent across age groups compared to the increase seen as age progresses in the general population.

U.S. Army male aviators showed a significant interaction effect for hematocrit levels [$F(3, 1191) = 9.88$, $P = 0.021$]. Pairwise comparisons showed that U.S Army male aviators ages 46–55 had significantly higher hematocrit levels compared to the U.S. general population ($P = 0.002$). U.S. Army male aviators showed significantly higher hemoglobin levels compared to the U.S. general population [$F(1, 1191) = 13.03$, $P < 0.001$]. U.S. Army female aviators had significantly higher hematocrit levels compared to the U.S. general population [$F(1, 1147) = 54.55$, $P < 0.001$]. U.S. Army female aviators showed a significant interaction effect for hemoglobin levels [$F(3, 1123) = 15.34$, $P = 0.002$]. Pairwise comparisons showed that U.S. Army female aviators had higher hemoglobin levels for age groups 16–25, 26–35, and 36–45 ($P < 0.001$ for all).

For total cholesterol, U.S. Army male aviators showed a significant interaction effect [$F(3, 1192) = 16.8$, $P < 0.001$]. Pairwise comparisons showed that male aviators ages 16–25 had higher cholesterol levels compared to the general population ($P = 0.013$), but male aviators ages 26–35 had lower cholesterol than the U.S. general population ($P = 0.024$). U.S. Army female aviators showed a significant interaction effect for total cholesterol [$F(3, 1150) = 9.71$, $P = 0.023$]; however, pairwise comparisons for each age group showed no significant differences between U.S. Army aviators and the U.S. general population ($P > 0.05$ for all).

Analysis of low-density lipoprotein revealed a significant interaction effect for men [$F(3, 1192) = 13.43$, $P = 0.005$]. Pairwise comparisons showed that LDL levels were significantly higher in U.S. Army male aviators compared to the U.S. general population for the 16–25 age group ($P < 0.001$). U.S. Army female aviators had significantly lower LDL levels compared to the general population [$F(1, 1149) = 5.33$, $P = 0.022$]. For HDL, U.S. Army male aviators had significantly higher levels compared to the U.S. general population [$F(1, 1192) = 30.34$, $P < 0.001$]. Comparatively, U.S. Army female aviators also showed significantly higher HDL levels [$F(1, 1145) = 231.33$, $P < 0.001$].

Furthermore, we incorporated analysis of the total cholesterol to HDL cholesterol ratio, a widely used cardiovascular risk stratification tool that compares relative levels of atherogenic lipoproteins to circulating concentrations of high-density lipoprotein particles.[19] The total cholesterol to HDL cholesterol ratio has been shown in multiple large cohort studies to predict incidence of coronary artery disease events and mortality independent of LDL cholesterol levels.[2,4,17] For U.S. Army male aviators, the total cholesterol to HDL ratio was significantly lower than the U.S. general population [$F(1, 1185) = 22.71$, $P < 0.001$]. For U.S. Army female aviators, a significant interaction effect was observed [$F(3, 1145) = 10.28$, $P = 0.018$]. Pairwise comparisons showed significantly lower ratio values across all four age groups ($P < 0.001$ for all). For triglycerides, no significant differences occurred in the male comparison groups. However, U.S. Army female aviators showed a significant interaction effect [$F(3, 1150) = 22.76$, $P < 0.001$]. Pairwise comparisons showed that U.S Army aviators ages 36–45 and 46–55 both had significantly lower triglyceride levels compared to the U.S. general population ($P < 0.02$ for all). Analysis of fasting blood glucose showed a significant interaction effect for both men [$F(3, 1183) = 8.13$, $P = 0.046$] and women [$F(3, 1131) = 17.88$, $P < 0.001$]. Pairwise comparisons showed that U.S. Army aviators had significantly lower glucose levels than the U.S. general population across all age groups and both sexes ($P < 0.001$ for all).

DISCUSSION

To be qualified for flight duty, U.S. Army aviators must meet strict physical fitness standards, pass a rigorous physical fitness test, and meet other U.S. Army standards defined in Chapter 4

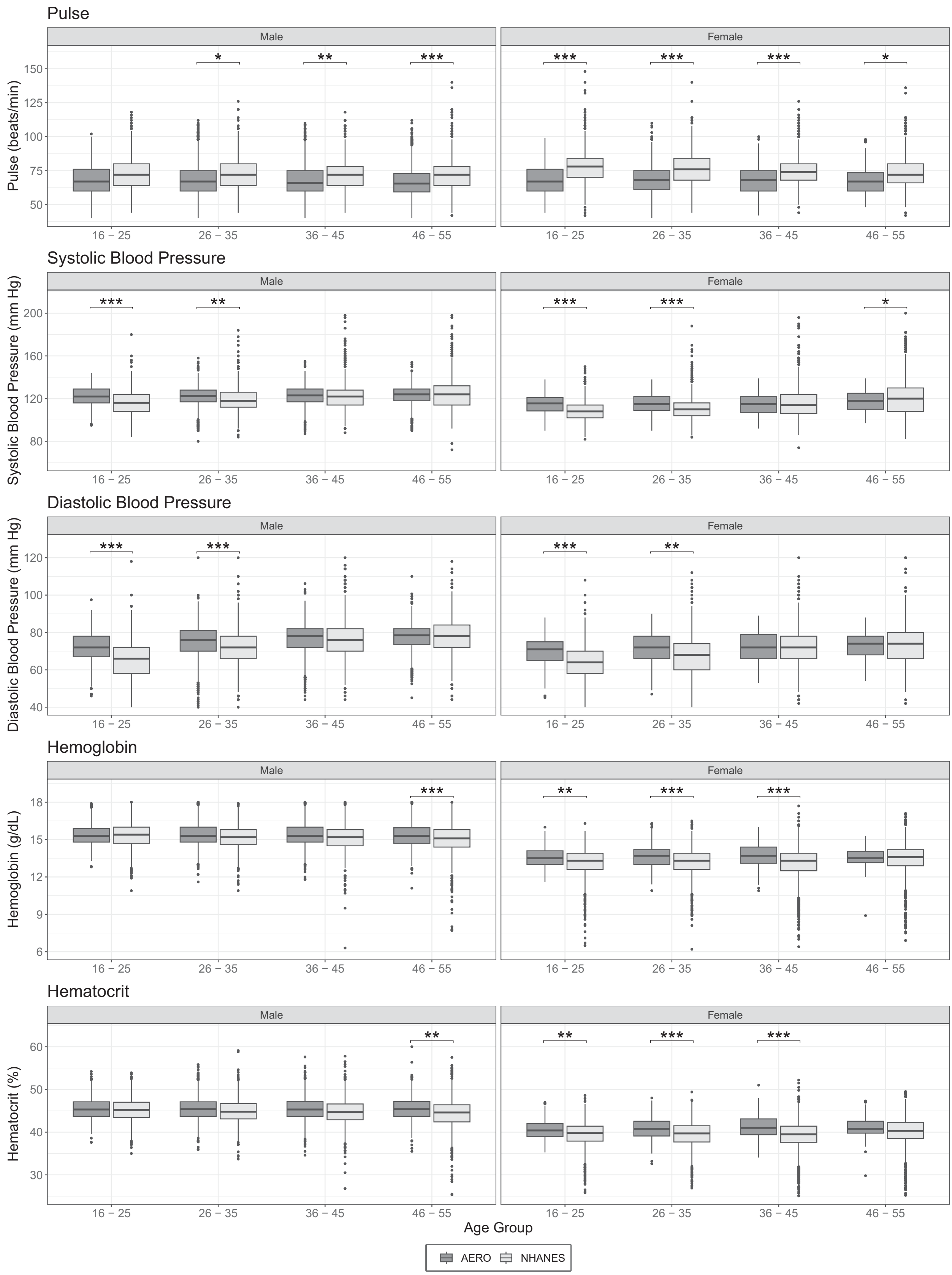

Fig. 1. Pulse, systolic and diastolic blood pressure, hemoglobin, and hematocrit box plots. This figure represents a standardized way of visualizing key statistical information about the distribution of quantitative data. The box encloses the interquartile range between the first and third quartiles, and the median is marked by a line inside the box. The whiskers extend to the minimum and maximum values in the dataset unless there are outliers. Outliers are data points (depicted by dots) that fall a specified distance above quartile 3 or below quartile 1 (1.5 times the interquartile range). The asterisks indicate the level of significance at the *P*-value levels of < 0.05, < 0.01, and < 0.001.

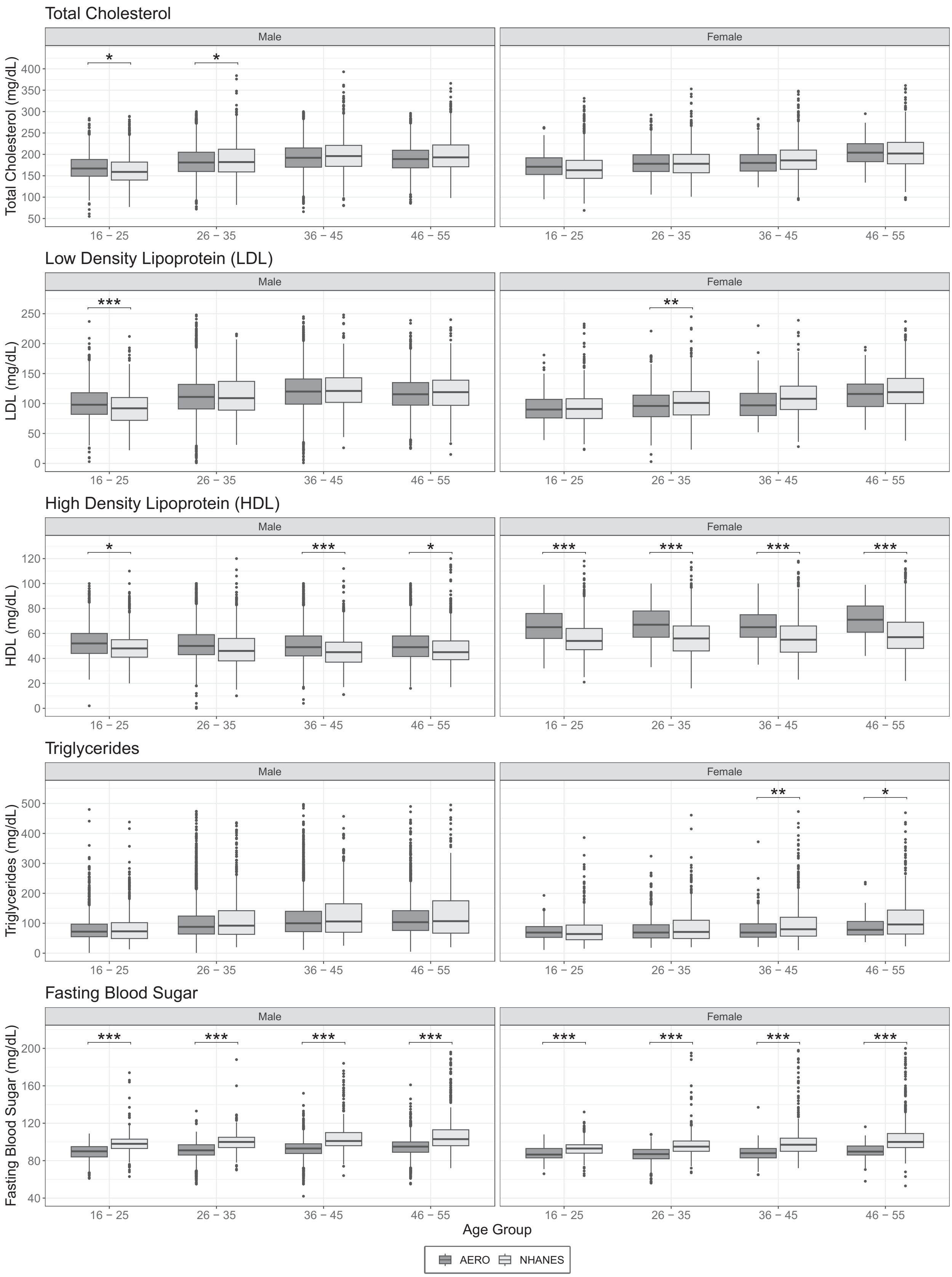

Fig. 2. Fasting blood sugar, total cholesterol, low density lipoprotein, high density lipoprotein, and triglyceride box plots. The box encloses the interquartile range between the first and third quartiles, and the median is marked by a line inside the box. The whiskers extend to the minimum and maximum values in the dataset. Outliers are data points (depicted by dots that fall a specified distance above quartile 3 or below quartile 1 (1.5 times the interquartile range). The asterisks indicate the level of significance at the *P*-value levels of < 0.05, < 0.01, and < 0.001.

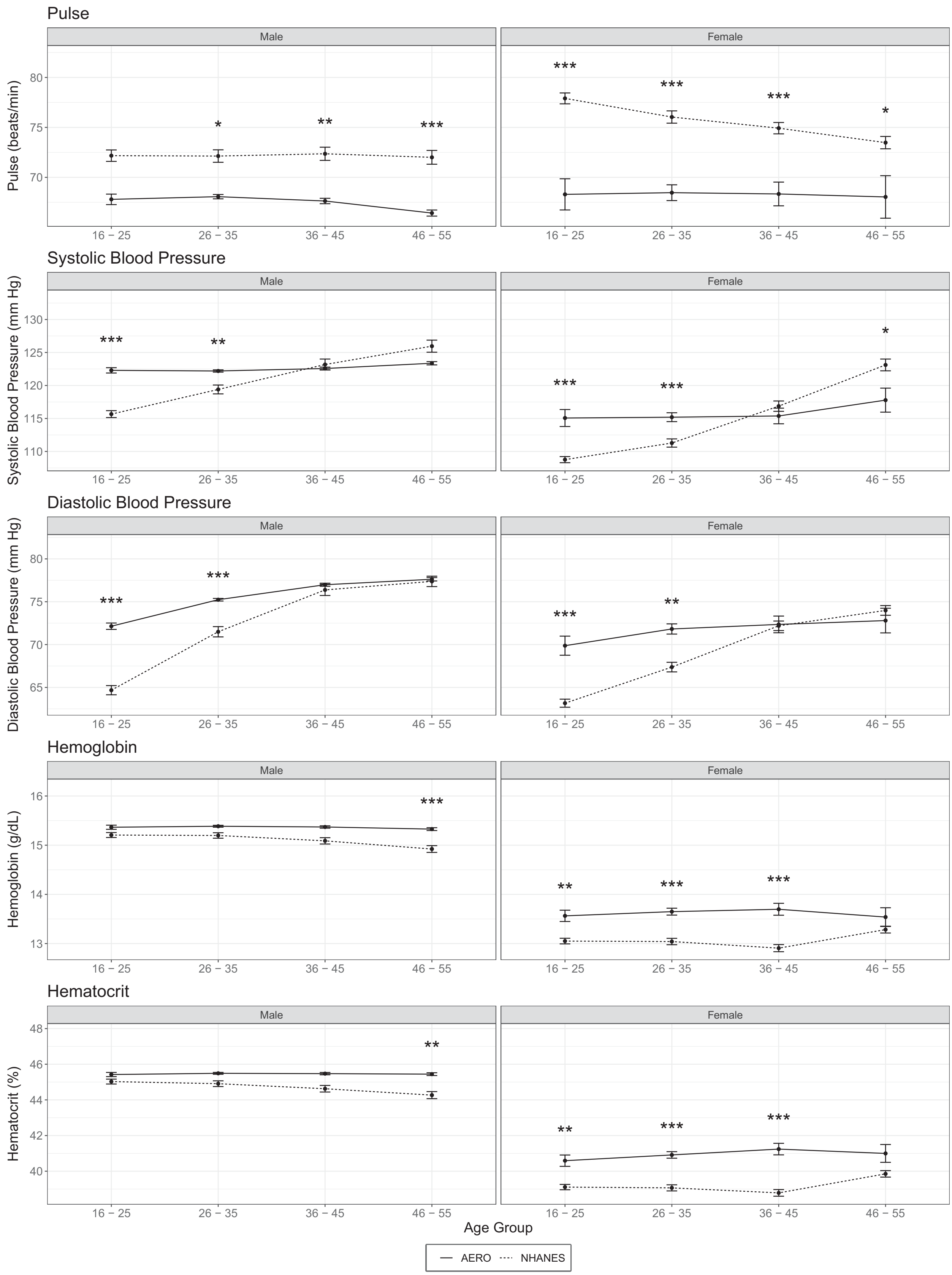

Fig. 3. Interaction plots of physiological metrics for pulse, systolic blood pressure, diastolic blood pressure, hemoglobin, and hematocrit. The data that is displayed is the mean response for two factors and their interaction. It allows for visual assessment to determine if the relationship between levels of one factor differs depending on the level of the other factor. The plots display the mean values for each factor level combination with error bars representing 95% confidence intervals. The asterisks indicate the level of significance at the *P*-value levels of < 0.05, < 0.01, and < 0.001.

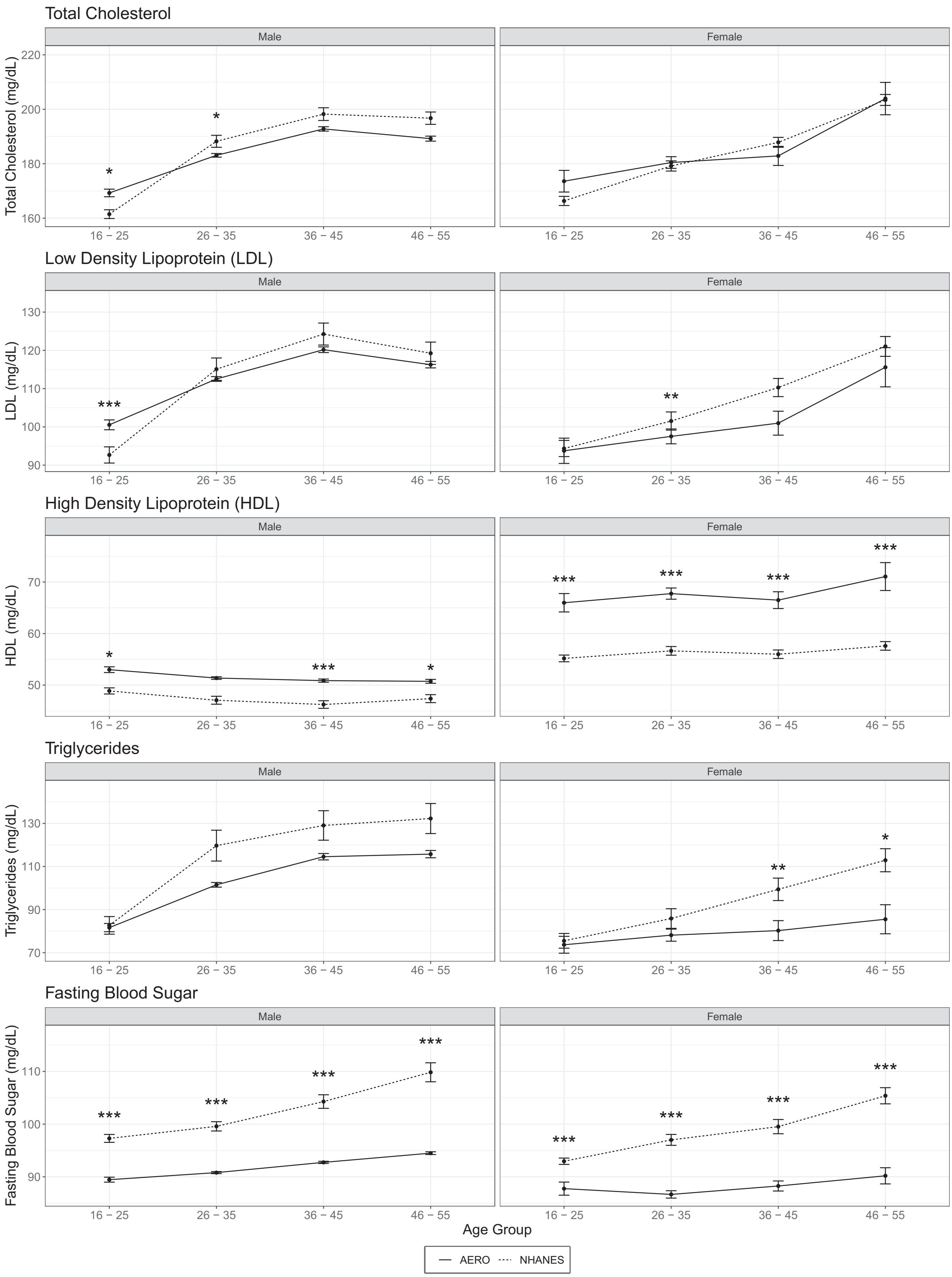

Fig. 4. Interaction plots of physiological metrics for total cholesterol, low density lipoprotein, high density lipoprotein, triglycerides, and fasting blood sugar. The plots display the mean values for each factor level combination with error bars representing 95% confidence intervals. The asterisks indicate the level of significance at the *P*-value levels of < 0.05, < 0.01, and < 0.001.

Table I. Tabular Representation of Physiological Metrics.

			SAMPLE SIZE		MEAN		STANDARD DEVIATION		
METRIC	GENDER	AGE GROUP	AERO	NHANES	AERO	NHANES	AERO	NHANES	*P*-VALUE
Pulse (bpm)	Male	16–25	1874	1606	67.80	72.17	11.60	11.70	0.068
		26–35	10,120	1259	68.06	72.13	11.19	11.31	0.024
		36–45	6588	1180	67.63	72.36	11.24	11.56	0.001
		46–55	4285	1235	66.42	72.00	10.16	12.40	0.000
	Female	16–25	212	1660	68.29	77.90	11.60	11.36	0.000
		26–35	742	1344	68.46	76.04	10.95	11.51	0.000
		36–45	287	1428	68.34	74.92	10.25	10.97	0.000
		46–55	108	1377	68.04	73.48	11.28	11.67	0.021
Systolic blood pressure (mmHg)	Male	16–25	1875	1547	122.29	115.66	8.91	10.53	0.000
		26–35	10,122	1221	122.20	119.40	8.76	12.00	0.007
		36–45	6590	1129	122.57	123.18	8.75	14.25	1.000
		46–55	4284	1178	123.37	125.96	8.21	16.05	1.000
	Female	16–25	212	1594	115.07	108.76	9.54	9.46	0.000
		26–35	743	1294	115.20	111.28	9.35	11.45	0.000
		36–45	287	1346	115.38	116.87	10.23	14.69	1.000
		46–55	108	1296	117.78	123.11	9.66	16.40	0.012
Diastolic blood pressure (mmHg)	Male	16–25	1875	1506	72.14	64.68	8.24	10.64	0.000
		26–35	10,121	1217	75.24	71.50	7.81	10.68	0.000
		36–45	6590	1130	76.98	76.38	7.38	11.18	1.000
		46–55	4284	1177	77.62	77.37	6.63	10.61	0.501
	Female	16–25	212	1577	69.87	63.16	8.29	9.52	0.000
		26–35	743	1288	71.82	67.37	8.27	10.26	0.007
		36–45	287	1344	72.35	72.19	8.42	10.41	1.000
		46–55	108	1294	72.80	73.98	7.63	10.39	1.000
Hemoglobin ($g \cdot dL^{-1}$)	Male	16–25	1578	1538	15.37	15.21	0.85	1.00	0.428
		26–35	8098	1234	15.39	15.20	0.88	1.00	1.000
		36–45	5386	1134	15.37	15.09	0.89	1.10	0.331
		46–55	3479	1222	15.33	14.92	0.86	1.23	0.000
	Female	16–25	172	1610	13.56	13.05	0.77	1.17	0.001
		26–35	602	1337	13.65	13.04	0.88	1.21	0.000
		36–45	234	1431	13.70	12.91	0.94	1.40	0.000
		46–55	86	1380	13.54	13.28	0.90	1.31	0.805
Hematocrit (%)	Male	16–25	1771	1542	45.42	45.03	2.51	2.75	1.000
		26–35	9334	1238	45.49	44.91	2.60	2.89	1.000
		36–45	6187	1139	45.47	44.63	2.63	3.17	0.358
		46–55	4058	1233	45.44	44.27	2.58	3.53	0.002
	Female	16–25	202	1610	40.59	39.11	2.30	3.07	0.007
		26–35	680	1337	40.91	39.06	2.44	3.19	0.000
		36–45	268	1431	41.24	38.78	2.70	3.61	0.000
		46–55	107	1380	41.00	39.85	2.64	3.46	0.070
Total Cholesterol ($mg \cdot dL^{-1}$)	Male	16–25	1843	1520	169.26	161.47	30.59	32.08	0.013
		26–35	9857	1231	183.08	188.24	33.78	39.53	0.024
		36–45	6508	1135	192.79	198.23	33.27	40.17	1.000
		46–55	4270	1216	189.22	196.73	30.67	40.38	1.000
	Female	16–25	209	1588	173.57	166.32	29.37	34.08	0.074
		26–35	734	1328	180.44	179.17	29.73	34.75	1.000
		36–45	287	1420	182.87	187.85	30.30	34.93	0.306
		46–55	108	1358	203.94	203.43	31.50	37.94	1.000
Low Density Lipoprotein ($mg \cdot dL^{-1}$)	Male	16–25	1839	696	100.54	92.66	28.18	28.46	0.000
		26–35	9865	504	112.52	115.08	31.29	33.51	1.000
		36–45	6502	533	120.17	124.26	30.50	33.87	1.000
		46–55	4268	557	116.26	119.25	28.08	35.05	1.000
	Female	16–25	209	706	93.75	94.35	24.37	28.66	1.000
		26–35	734	608	97.52	101.53	26.86	29.89	0.004
		36–45	288	623	100.97	110.29	27.09	30.22	0.750
		46–55	108	634	115.58	121.03	27.14	33.33	1.000

(*Continued*)

Table I. (*Continued*).

METRIC	GENDER	AGE GROUP	SAMPLE SIZE AERO	SAMPLE SIZE NHANES	MEAN AERO	MEAN NHANES	STANDARD DEVIATION AERO	STANDARD DEVIATION NHANES	*P*-VALUE
High Density Lipoprotein ($mg \cdot dL^{-1}$)	Male	16–25	1834	1520	52.99	48.87	12.18	11.84	0.021
		26–35	9820	1231	51.36	47.06	12.58	13.76	0.059
		36–45	6471	1132	50.87	46.23	12.85	12.66	0.000
		46–55	4253	1215	50.73	47.37	12.59	13.74	0.017
	Female	16–25	204	1587	65.98	55.18	12.99	13.24	0.000
		26–35	706	1324	67.76	56.64	14.74	15.65	0.000
		36–45	280	1418	66.49	55.99	13.90	15.81	0.000
		46–55	103	1352	71.06	57.61	14.01	15.70	0.000
Triglycerides ($mg \cdot dL^{-1}$)	Male	16–25	1844	653	81.64	82.68	42.11	53.25	1.000
		26–35	9875	496	101.50	119.68	54.71	81.33	1.000
		36–45	6512	515	114.54	129.04	61.14	79.21	0.235
		46–55	4273	537	115.74	132.25	56.55	82.37	1.000
	Female	16–25	209	682	73.69	75.52	28.88	45.59	0.120
		26–35	734	584	78.14	85.86	38.74	56.28	1.000
		36–45	288	603	80.26	99.40	40.03	65.27	0.002
		46–55	108	621	85.52	112.90	35.75	67.95	0.016
Fasting Blood Sugar ($mg \cdot dL^{-1}$)	Male	16–25	1223	661	89.45	97.29	8.39	9.83	0.000
		26–35	7009	502	90.79	99.58	8.32	10.10	0.000
		36–45	6305	512	92.74	104.28	8.47	14.86	0.000
		46–55	4269	520	94.49	109.84	8.80	20.96	0.000
	Female	16–25	143	689	87.75	92.95	7.57	8.02	0.000
		26–35	552	585	86.65	97.01	8.38	12.76	0.000
		36–45	280	591	88.25	99.52	8.15	16.77	0.000
		46–55	108	610	90.19	105.38	8.15	19.33	0.000

Tabular representation of physiological metrics between groups for pulse, systolic blood pressure, diastolic blood pressure, hemoglobin, and hematocrit and lipid profiles. Summary statistics are representative of all available data and *P*-values are derived from the reduced data set.

of Army Regulation 40-501.[22] These requirements likely contribute to their physical fitness and well-being. However, aviators encounter many environmental stressors that can have a negative impact on health, such as high altitude, noise, and vibration.[7] Nonetheless, some research suggests that the stressors also promote physiological adaptations that improve overall health, such as increased red blood cell production, which improves tissue oxygen delivery, as a result of the stressor.[26] In addition to these factors, genetic factors and individual differences must be taken into consideration. Some people have a genetic predisposition to be more physiologically fit than others,[12] and it is plausible that people who seek aviation careers may have a genetic makeup that renders them healthier than the general population. Furthermore, the healthy worker effect, a type of selection bias that occurs in occupational cohort studies, can lead to an underestimation of the risks associated with certain occupations and is especially applicable to the comparisons made in this study.[21] Any U.S. Army aviator who does not meet standards is likely to be identified and removed from the workforce, which can skew the results of studies that compare the health of aviators to the general population.

Our study compared the physiological measurements of U.S. Army aviators to those of the U.S. general population to assess if the aviation population is truly "more physiologically fit" than the U.S. general population. U.S. Army aviator flight physical data from the AERO database were compared to age, time, and biological gender-grouped data from the CDC NHANES database. The results of this study showed that there were statistically significant differences between U.S. Army aviators and the U.S. general population in many physiological metrics. Key metrics like pulse rate and fasting glucose were consistently lower in U.S. Army aviators across age and gender. This implies U.S. Army aviators have physiological advantages that may reduce their risk of chronic cardiovascular and metabolic diseases. Maintaining ideal physical fitness and body weight promotes cardiovascular endurance and resilience.[14] Hence, U.S. Army aviators may perform duties safely for longer durations under high stress compared to the general population. However, a nuanced perspective is warranted, as some parameters like cholesterol and blood pressure showed less consistent differences.

Though aviation demands can initially induce adaptive responses like lowered heart rate, occupational stresses over time negatively impact other physiological measures. In particular, chronic noise exposure is a well-documented hazard faced by aviators that distinguishes them from the general population. Persistent loud noise from aircraft engines has been shown to contribute to hearing loss and tinnitus among pilots. This is likely the primary domain where aviators physiologically diverge from the public due to direct occupational environmental exposure.[13] Additional effects of vibration and altitude changes include increased blood pressure and hematocrit production over time, which may plateau at subclinical levels or become pathological after years of service without intervention.[1] Some research also indicates aviators experience more spinal issues like low back and neck pain later in their careers, partially due to vibration exposure.[10] While aviation may confer initial cardiovascular benefits, certain exposures produce measurable declines not faced by the nonflying population, especially in hearing, but also potentially in blood composition, spine health, and other areas. This highlights the need for monitoring tailored to aviation hazards over the career span.

Overall, while this study shows some selective advantages for aviators, it does not fully support the assumption that they are "generally healthier" across all cardiovascular and metabolic markers. For example, U.S. Army male aviators showed minimal differences compared to the U.S. general population with respect to LDL, cholesterol, triglyceride, hemoglobin, and hematocrit measurements across the various age groups. Hence, targeted initiatives to optimize physiological fitness may be beneficial, but close monitoring of aviators over their career is still warranted to detect negative impacts of flight on specific health parameters. Rather than making broad generalizations, it would be prudent for U.S. military health policy makers to take a more measured approach based on regular health assessments of U.S. Army aviators. Areas like pulse rate, where aviators show clear advantages, can be maintained with physical fitness training. Parameters like blood pressure, where U.S. Army aviators appear comparable to (and in some groups higher than) the U.S. general population, may require routine monitoring and management. A balanced, evidence-based approach accounting for the impacts of flight will optimize aviator safety, health, and performance.

This study has several limitations. First, it is a retrospective study, which introduces a risk of bias. The study only looked at U.S. Army aviators, so it is unclear if the findings apply to other military aviators or Army soldiers in general. The study is cross-sectional in design and, although it did include age-banding, the study did not follow individuals over time to see how their overall physiological profiles changed. The retrospective data points were drawn from the AERO database, which has inherent constraints limiting the breadth and depth of analysis. Specifically, the dataset's narrow focus on aviation-specific metrics and its limited number of physiological parameters restricts the ability to derive significant insights about broader health or performance outcomes. The study did not control for other factors influencing health, such as diet, smoking, or exercise. The reasons for the differences obtained are not fully understood. However, they may be due to a combination of factors, including the rigorous physical fitness standards that aviators must meet, the environmental stressors they are exposed to, and their lifestyle choices.

Importantly, as briefly mentioned previously, a significant limitation of our study is the lack of data on smoking rates and behaviors within both the U.S. aviation and U.S. general population samples. Smoking has well-established effects on cardiovascular parameters like blood pressure and hematologic markers that could influence the differences observed between groups. Without controlling for smoking, we cannot definitively conclude that higher blood pressure and hematocrit levels among aviators relate to superior fitness or occupational stresses rather than simply reflecting higher smoking prevalence. The omission of smoking data hampers the ability to characterize overall health advantages and weakens arguments regarding adaptive or maladaptive responses to aviation hazards. The lack of correlation with smoking behavior is a major shortcoming that restricts the interpretability of our findings. Future studies should capture smoking rates and incorporate this data into analysis to permit appropriate conclusions regarding cardiovascular health, hematologic impacts, and overall fitness. Controlling smoking would greatly strengthen the evidence available to military health policymakers in optimizing aviator standards and safety initiatives relating to flight physiology.

Moreover, the CDC NHANES database uses a stratified, multistage, probability-cluster sampling design. This approach intentionally oversamples certain demographic groups, including older adults, African Americans, and Hispanics. The oversampling ensures sufficient data is collected from these groups to yield representative sample sizes reflecting their proportion in the overall U.S. population based on census data. It accounts for anticipated noncompliance and nonparticipation rates within each stratum. In this way, oversampling typically underrepresented groups enhances the probability of obtaining an adequately sized sample to reflect the true national demographic distribution. The resulting dataset provides a representative portrait of the population, not an overrepresentation of the oversampled groups.

Our retrospective analysis provides a statistical comparison between U.S. Army aviators and the U.S. general population, assessing many physiological variables that aid in assessing cardiovascular health, metabolic, and lipid profiles. Our study suggests that the current regulations and Aeromedical Policy Letters are effective at promoting physiological advantages for U.S. Army aviators to help lower their risk for developing cardiovascular disease, diabetes, and other chronic diseases compared to the U.S. general population. Importantly these findings draw attention to the need to evaluate all physiological metrics in a systematic fashion. Interestingly, the data did not reveal comprehensive health advantages across all metrics examined. Taken together, these findings indicate a nuanced relationship between aviation and physiological fitness. The requirements of U.S. Army aviation appear to promote cardiovascular endurance and metabolic health but may not lead to global improvements across all health parameters. Targeted monitoring and maintenance initiatives may be warranted to optimize aviator physiological fitness over a career span, particularly to detect potential negative impacts of occupational stresses over time.

Although we cannot definitively attribute these findings to any individual or group of specific variables, our results are likely due to numerous factors, including but certainly not limited to the strict physical fitness standards that U.S. Army aviators must meet, the environmental stressors they encounter, and the regulatory environment of accession and retention standards that apply throughout their career. The findings of this study also have several implications for U.S. military health policy. For example, the findings support ongoing review and evidence-based modification of medical standards to optimize health outcomes (adding emerging metrics like heart rate variability that better predict overall physiological status). The results highlight the need for more targeted monitoring and maintenance programs to mitigate potential negative effects of aviation stresses over time. This could include more frequent or in-depth hearing tests, spinal health checks, blood pressure monitoring, etc., based on an analysis of aviation-specific risks.

Furthermore, the results suggest the possibility of adjusting fitness standards to be more specialized to the physical and mental demands of flying rather than general fitness benchmarks. This could help attract and retain aviators with capabilities optimized for the aviation environment. Moreover, this study provides impetus for further research into other potential health impacts of aviation service and additional metrics that may offer early warning signs of subtle declines, for example, detailed studies on effects of vibration, noise, fatigue cycles, etc. However, it is essential to note that this study only examined a limited number of physiological metrics currently monitored according to medical standards. In addition to the physiological metrics in this study, future research should consider other factors to gain a full picture of overall health. Furthermore, researchers could consider other factors when assessing the overall health of aviators, such as heart rate variability, respiratory function, and real-time operator state. Finally, this study reinforces the importance of ongoing qualification standards in ensuring the aviation population is shaped toward health and supports periodic review of disqualifying conditions based on current evidence.

Other factors to evaluate when assessing overall health include individual physiological trends, mental health, sleep quality, smoking, and nutrition. Future studies should examine these factors to get a more comprehensive understanding of the health of aviators. Aviators, over their lifetime, may maintain "normal" physiological metrics and year-to-year trends should be considered when evaluating an individual's health status. Mental health is essential to consider as aviators experience stressful situations that can negatively impact their mental health.[13] Sleep quality is also important, as sleep deprivation can impair cognitive function and increase the risk of mishaps.[1] Nutrition is another critical factor, as aviators must maintain a healthy diet to optimize their performance.[10] By considering these factors, we can better understand an aviator's health status and develop more effective strategies for improving or maintaining their health and well-being.

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Authors and Affiliations: Matthew D'Alessandro, Ph.D., CPT, Samantha Wolf, D.O., CPT, and Ian Curry, M.D., COL, Warfighter Performance Group, Ryan Mackie, M.S., Oak Ridge Institute for Science and Education, U.S. Army Aeromedical Research Laboratory, and James S. McGhee, M.D., M.P.H., Department of Aviation Medicine, Oak Ridge Institute for Science and Education, Fort Novosel, AL, United States.

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Free Cognitive Capacity Assessed by the P300 Method During Manual Docking Training in Space

Juri Akardevic Bubeev; Bernd Johannes; Tatyana I. Kotrovska; Darya Schastlivtseva; Sergey Bronnikov; Hans-Juergen Hoermann; Anthony W. K. Gaillard

INTRODUCTION: The classical P300 brain potential method was used to assess the cognitive capacity during training of manual docking in space. The aim of the study was to enhance the safety of this operation during a mission.

METHODS: To examine this, $N = 8$ cosmonauts had to perform the manually controlled docking task simultaneously with an acoustic monitoring task. The P300 component was evoked by the acoustic stimuli of the secondary task. The docking task had to be executed at three difficulty levels: low (station not turning); medium (station turning around one axis); and difficult (station turning around three axes). In the secondary task, subjects had to discriminate between a low and a high tone, which occurred with a probability of 90% and 10%, respectively. Subjects had to count the high tones. After the 10th high tone, they had to inspect the power supply by giving an oral command.

RESULTS: A methodology for event-related potentials was successfully demonstrated under space conditions. The P300 amplitude was largest and the latency shortest during the medium difficult task.

DISCUSSION: The results suggest that P300 can be recorded during the complex manual docking task in space and could be used to assess individual available cognitive capacity of cosmonauts during a space mission.

KEYWORDS: manned spaceflight, manual docking, secondary task, available cognitive capacity, P300 brain potential.

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Occasionally, we are reminded that human spaceflight is far from being routine. For example, when in 1997 the Soyuz TM-25 spacecraft with the German astronaut Reinhold Ewald on board was approaching the Mir space station, a few meters before contact the automated control system was disengaged because of a misalignment with the docking port. The commander took control and performed a successful manual docking. British astronauts Helen Sharman on board Soyuz TM-12 in 1991 and Timothy Peake with Soyuz TM-19M in 2015 had the same experience. The "Kurs" docking navigation system failed on the final approach and manual docking had to be performed to prevent accidental damage or a catastrophic outcome.[26] These and further safety-related occurrences with the remotely operated Progress freighter[28] confirm the significance of training cosmonauts and astronauts in manually controlled docking operations. Manually controlled docking of a spacecraft is a challenging and critical maneuver during space missions[18] because the cosmonaut/astronaut has to control the spacecraft's movements with six degrees of freedom. Three control devices and a two-dimensional display serve this purpose.[11] Moreover, Salnitski[24,25] observed during the Russian Mir missions that manual control performance eroded due to lack of training over 60 mission days such that the safety of a docking maneuver could be jeopardized. Therefore, Manzey[16] recommended continuous performance monitoring in space. Psychophysiological measurement, such as the electroencephalogram (EEG), have proven sensitivity to levels of attention and cognitive activities of humans.[19] An assessment of theta waves

From the Science State Scientific Center of the Russian Federation, Institute of Biomedical Problems of the Russian Academy of Sciences, Moscow, Russian Federation; the German Aerospace Center, Cologne, Germany; Rocket and Space Corporation "Energia" S. P. Korolev, Korolev, Moscow Region, Russian Federation; and Tilburg University, Tilburg, Netherlands.

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Address correspondence to: Hans-Juergen Hoermann, Ph.D., Sportallee 54a, Hamburg 22335, Germany; hans.hoermann@dlr.de.

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with the EEG in space[13] indicated differences between mission phases and was related to decreased alertness even during a simulated docking task in space. Herein we focused on another EEG approach—assessing event-related potentials (ERPs).

Reliable human performance requires extra cognitive resources that can be devoted to unexpected demands which might occur during a task execution.[6,12,27] Several EEG methods have been applied in secondary task settings on the ground.[1,7,15] To gauge free cognitive capacity, a secondary task was added to the main task, which evoked a positive ERP around 300 ms, called P300 or P3.[22] A comprehensive summary of studies examining ERPs in relation to varied cognitive task demands can be found in Prinzel et al.[23]

In previous studies,[8,10] we found that P300 indicated the free cognitive capacity during training of a spacecraft docking maneuver. We applied a secondary task[4,17] that was realistically embedded into the docking maneuver scenario. As Bubeev et al.[3] ascertained, the nature of the dual-task design is essential for the cosmonaut's motivation to commit to such research. The cosmonaut's enthusiasm increases with the perceived mission relevance of the tasks. Therefore, the secondary task was framed as part of adjusting solar panels toward the sun. In this study, we tested whether a secondary task implemented in a docking task with the space-certified equipment Neurolab-2010[11] evoked a reliable P300 under space conditions. A key condition for a reliable P300 assessment is a reliable EEG. The research was conducted as the final step of developing a space application after many years of preparatory international cooperation on the ground.

METHODS

Subjects

Eight male Russian cosmonauts participated in this study. They were between 34 and 54 yr old (mean 46 ± 7.3 SD) with a body mass index of 27 (± 2.7 SD) kg · m^{-2}. This space experiment, "PILOT-T", was approved both by the local internal review board (Institute of Biomedical Problems) and the Human Research Multilateral Review Board (for International Space Station experiments).

The German participation in the experiment was approved by the Ethics Committee of the Medical Association North-Rhine in Düsseldorf, Germany. Written informed consent was obtained from all subjects.

Procedure

Subjects were trained in manual docking according to the standard educational procedure in the beginning of their professional career as cosmonauts. The "easy" task simulates the standard setting of a manually controlled spacecraft docking maneuver at a space station. The spacecraft is located abeam the docking point, the subject was looking at the point of contact. The spacecraft had to be flown sidewards in a 90° curve, maintaining a safety distance until stabilized at the centerline, and finally approaching and docking port. In the standard setting the space station is fixed relative to the spacecraft. The experimental tasks were identical to earlier studies in previous publications.[2,9] In the first two tasks the cosmonauts had to perform the easy task (data aggregated as "easy"), which required flying in the x-plane, resembling horizontal conditions on Earth. These tasks simulate realistic operational training; the station was stable, as for regular standard training of the cosmonauts. The "medium" task required flying in the x-y plane (vertical) and turning down. With respect to the degrees of freedom, the medium difficult task was physically identical to the easy task but mentally more demanding, because humans living on Earth are usually not familiar with such movements. In the "difficult" tasks the station was rotating, with fixed rotation speed and two rotating axes. In this third condition the target turned around the y-axis faster and additionally turned constantly around its x- and z-axes.

The docking performance was evaluated by a factor analytical approach, described in detail by Johannes et al.[11] Exploratory and confirmatory factor models were verified in 10 independent subcohorts; the vector sums of the scores in underlying factors were adopted as integrated performance scores. A set of discriminant functions made these factor models applicable to the actual data.

A series of tones, in two different pitches (750 and 1000 Hz), were presented to the cosmonauts via headphones (presentation time 50 ms, volume 80 dB, interstimulus interval fixed 2.2 s). The relevant tone was higher than the irrelevant tone and occurred less often, 1 time out of 10 tones. To make the secondary task more authentic to the cosmonauts, we related the task to the monitoring of the battery power. Subjects had to count the high tones and switch to the solar panel system; when 10 high tones were detected, they had to give the voice command "переключить" (switch). We used voice commands to avoid interference with the manual docking task. The number of incorrect reactions was counted as errors in the secondary task. If the subjects reacted too early (for example already switching after the eighth tone), the error score would have the absolute value of "−2". Vice versa, if they reacted too late (e.g., 12th tone), the error score was "2."

The sampling plan was defined by the operational restrictions of spaceflights. The number of subjects from the space agency was eight. The number of experiments (sessions) corresponded to the standard of spaceflights. Preflight an additional training session without registrations was run. In this familiarization session the same conditions were given as in the experimental session. The primary goal was to familiarize the subjects with the secondary task, and with the use of voice commands. The experiment was run during the three flight phases: preflight (three sessions in the training center on the ground 14 d prior to departure with 3 intersession days), in flight (half year, one session each second week in space in the space station), and postflight (two sessions in the training center on the ground 1 and 3 d after landing).

In each session, the subjects had to perform five tasks, two with the easy condition, one with the medium condition, and two with the difficult condition. The data obtained in the two easy conditions and in the two difficult conditions were combined.

The Neurolab-2010 and the hand controls that resemble those used on the Russian Soyuz for docking on the International Space Station were developed and produced for space applications by Koralewski Industrie Elektronik oHG, Hambühren, Germany. The complete software package to manage the measurement systems was developed by SpaceBit GmbH, Eberswalde, Germany. The core module (which has been in space since 2015) controlled the entire communication with the experimental computer via USB interface and registered all electrophysiological parameters. Due to the limited sanitary conditions on the space station, cosmonauts often rejected wet electrodes. Therefore, we used dry electrodes. Either 8 or 19 electrodes (Standard 10-20) provided reliable EEG signals of high quality. The reference electrode was placed between Fp1 and Fp2, and the ground electrode was located between Fp1 and F7. Impedance was kept below 50 kΩ by applying drops of water. EEG was registered with a sample rate of 500 Hz, gain = 22,000, and 24-bit digitalization depth using an ADS 1299 chip from Texas Instruments at gain level 12 (22,878 digits/mV). Data were filtered with 0.5-Hz high pass and 20-Hz low pass frequencies. We had to exclude the very first dataset preflight due to technical problems.

Statistical Analyses

To develop an autonomous onboard analysis and feedback loop of the EEG results, the R system was used (R3.5.2, package nlme, R Foundation, Vienna, Austria). The EEG channels were examined for whether they successfully passed a signal quality check, including peak-to-peak moving window artifact detection (ERPLAB[14]). To obtain robust and reliable data, the ERPs were averaged across channels. Because the Cz-channel at the middle of the skull (Vertex) is a standard for ERP studies under laboratory conditions, these data were compared to the averaged ERPs of the other channels. For a more reliable P300 assessment difference waves (DWs) were calculated.[5] The ERPs for the irrelevant tones were subtracted from the ERPs for the relevant tones. Finally, the EEG responses were averaged separately for relevant and irrelevant tones.[6,21]

The following measures of the P300 were obtained. Latency is the time between the presentation of a tone and the start of the P300 component (in a window of 200–450 ms), which indicates that our brain has discriminated between a high and a low tone; this is the start of the P300 and the end is when the two curves come together again. Amplitude is the maximum peak (μV) in a window of 200–500 ms. Magnitude is the area (μV) between the beginning of the P300 and the end of the P300 and the largest peak, similar to the amplitude in a window of 200–500 ms. The statistical analyses of the data were done with the SPSS IBM package (vs. 21; IBM, Armonk, NY, United States). Correlations between performance parameters were estimated by Spearman's rho. Linear mixed effect models were developed to test the statistical significances of the independent variables flight phases and task difficulty as fixed effects.

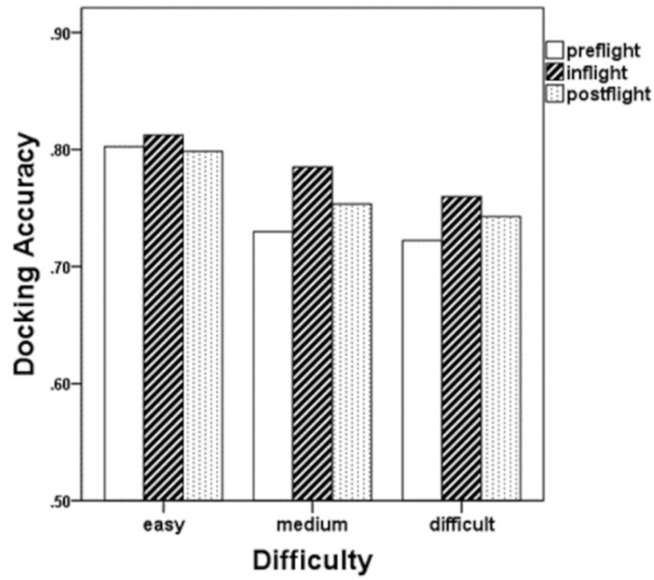

Fig. 1. Docking accuracy as a function of difficulty and flight phase.

RESULTS

The docking performance for the three flight phases is illustrated in **Fig. 1**. The accuracy of docking decreased at the higher difficulty levels for each of the flight phases. The accuracy pattern remained nearly the same across all three flight phases.

When the difficulty increased, the docking accuracy decreased (Spearman's rho = –0.337, $P < 0.001$, Fig. 1); also, the performance accuracy was significantly different between flight phases [F(num:2, denum: 354.781) = 3.935, $P = 0.020$] and levels of difficulty [F(num: 2, denum: 353.539) = 13.071, $P < 0.001$].

In flight, 121 responses to the secondary task were counted for all 134 flights. **Fig. 2** presents the number of errors in the

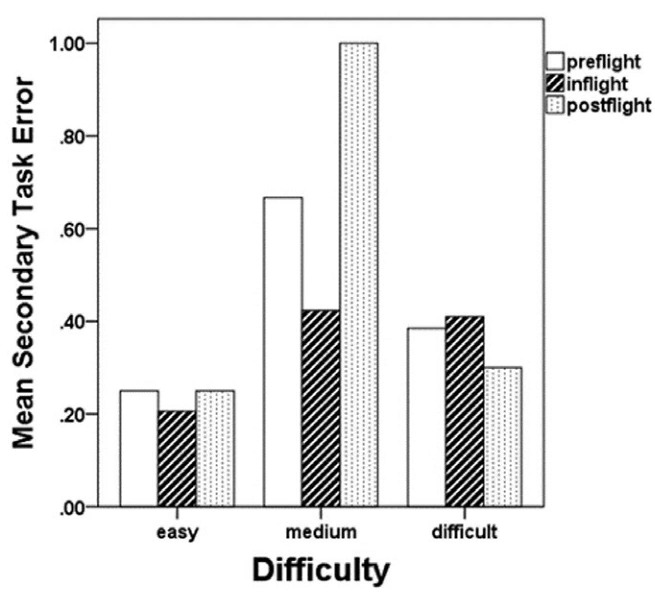

Fig. 2. Number of errors in the secondary task as a function of flight phase and task difficulty.

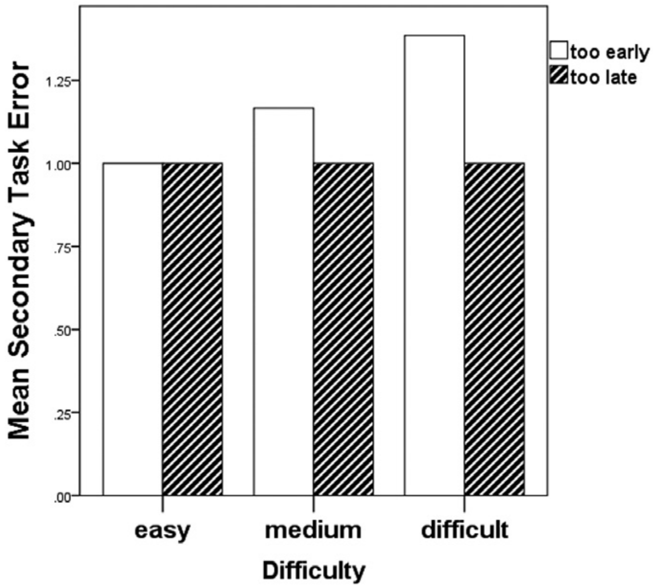

Fig. 3. Type of error in the secondary task in relation to task difficulty.

secondary task, switching the system "too early" (16.54%) or "too late" (13.81%). Most responses (69.65%) were made in time.

The number of errors in the secondary task clearly increased with task difficulty. In general, subjects tended to react too early. The low number in the "correct" category is due to the coding of "correct" errors with "0." In general, subjects tended to react too early (**Fig. 3**).

Secondary task performance was not correlated with docking accuracy. The secondary task performance was extremely high; the task may have been too easy for the subjects. The number of errors, too early or too late, increased with docking difficulty. However, the accuracy differences were not correlated with differences in secondary task performance.

We had to exclude the very first dataset, preflight, due to technical problems. The effects of combining EEG channels were analyzed. A comparison of ERPs which were averaged over 8 or 19 channels with those which were obtained from the Cz alone showed sufficient similarity. An averaged correlation of 0.94 was found preflight for the standard task (easy); in flight the respective averaged correlation was 0.89. However, postflight measures were worse and not significantly correlated.[1]

Fig. 4A, B, and C present the EEG DWs. The ERPs to the lower tones were subtracted from the higher tones[5] separately for the three flight phases: preflight, in flight, and postflight, and during easy, medium, and difficult docking tasks. **Table I** presents the averaged DW magnitude values of the P300. In general, the DWs were similar among flight phases as well as among difficulties.

The latencies were assessed in the area between 200–450 ms. P300 amplitudes and magnitudes were measured in a larger window (200–500 ms).

Magnitude is an area measure. The differences between difficulties as well as between flight phases were tested for significance. For the EEG data the most popular analysis of variance could not be applied because the premise of the normal distribution of the input data could not be statistically confirmed. Therefore, we decided to use nonparametric tests without the limitation of distribution. For a dependent data analysis (Friedman test), the data had to be averaged by subject, condition, and measurement points to have equal amounts of data. The independent analysis (Kruskal-Wallis) will ignore the subject's dependency. However, all three analysis types provided highly significant results confirming each other. So, we will present only a summarizing verbal evaluation.

The P300 magnitude differed highly significantly ($P < 0.001$) between the difficulty levels during preflight and in flight, but not at all during postflight experiments. It also differed highly significantly between all flight phases. Between in-flight and postflight experiments the significance level was slightly lower: $P = 0.004$ (still highly significant). Reducing the information to a set of parameters per P300 reduces the statistical power so drastically that nearly no significances were left in all comparisons except for the P300-slope.

The number of stimuli depended on the individual flight duration and differed between task difficulties and subjects. The average number of ERPs for relevant stimuli was 124 for the easy tasks, 71 for the medium tasks, and 150 for the difficult tasks.

The P300 of the DWs were visually existent in all three task conditions. However, the P300 magnitude did not differ significantly between difficulties as a single value per ERP. There were also no differences in latency between task difficulties or between Flight Phases. For the slopes, we found a significant ($P = 0.046$) difference among difficulties, indicating a steeper slope during the medium difficult tasks. No slope-differences were found among flight phases.

DISCUSSION

This experiment was the latest attempt in a Russian-German Joint project to use in-space electroencephalographic measures for diagnostic purposes for workability of cosmonauts during a mission. The data were obtained with three generations of a system named "Neurolab-B," "Neurolab-2000," and "Neurolab-2010." The first joint experiment in space was realized in 1996.

The main result of the herein presented experiment are not any statistically surprising new relations between, e.g., performance and physiological correlates, but the successful application of a P300 methodology in space during a highly complex operational task, first applied in 2008. This may become of high relevance in future attempts to evaluate cosmonauts' readiness and proficiency while manually docking a spacecraft in space on a station, eventually very autonomously and far from Earth, supported by onboard expert systems.

EEG signals are highly sensitive to several environmental and behavioral factors. By averaging of channels, it was intended to accumulate the reliable variations across all data. We compared our "averaged" channels with the standard Cz channel. The results confirmed a wide range of variability, but

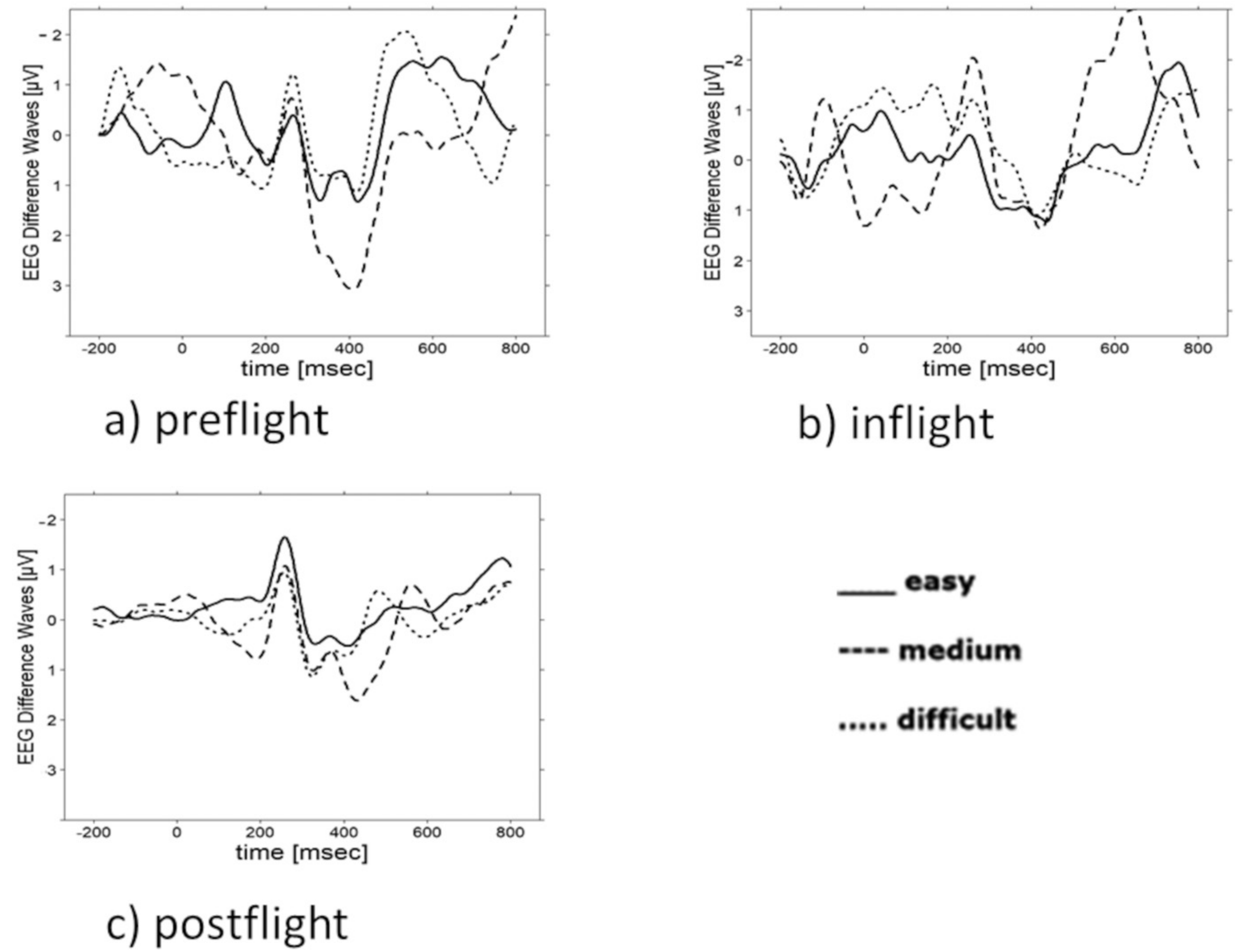

Fig. 4. EEG difference waves for the flight phases and levels of difficulty.

also a good chance to substitute the single channel measure Cz by an averaged, more stable measurement. With this presented EEG methodology, we found several important results which provide information on human's workability, especially as an indicator of available cognitive capacity. This could be used, for example, as a quick first feedback to the operators about their current performance and mental state.

Table I. DW Magnitudes in µV of the P300 Component (Range 200–500 ms).

FLIGHT PHASE & DIFFICULTY	MAGNITUDE (µV)	MP/TRIALS	SD
Preflight			
easy	0.0233	1963/13	0.12682
medium	0.1938	1963	0.30869
difficult	0.0072	1963	0.10468
In flight			
easy	−0.0068	12,533/83	0.15423
medium	0.0303	12,533	0.15969
difficult	0.0074	12,533	0.14886
Postflight			
easy	0.0260	2416/16	0.11930
medium	0.0029	2416	0.17162
difficult	−0.0013	2416	0.10691

MP: measurement points of ERP-segment - 501 MPs per event-related potential (ERP); Trials: number of included ERP-trials.
Correlation values can be provided upon request.

Overall, the acquisition and analysis of these data were successful. Despite the methodological restrictions in space, it was possible to apply the P300 methodology to assess free cognitive capacity during docking training. Our study confirms that the method of combining dual tasks and evoked brain potentials is suitable for assessing an operator's cognitive spare capacity in operationally relevant tasks under laboratory terrestrial conditions[20] as well as in space. On Earth several studies demonstrated that P300 was affected by the difficulty of the primary task.[6,12] The same was observed in space.

Real docking in space is a prime example of a professional task where poor operator performance is likely to result in catastrophic consequences. Self-evaluation alone is not sufficient for judging one's readiness for proper task performance.

Usually, P300 is visually inspected and manually analyzed. Such an approach is time consuming and cannot be used to provide immediate feedback regarding free cognitive capacity for cosmonauts in space. Instead, software tools based on intra-individual statistical analyses could provide immediate feedback on board in the context of performing the docking task.

One limitation of our study is the limited number of subjects. However, the carried-out effort and the reported results recommend pursuing this research to further develop this prototype application for practical usage in space with an improved data analysis procedure. The present status of the automated data analysis already supported the scientific work, but still required too much interaction with the researcher.

The findings should be further confirmed in independent samples under real or simulated space conditions (such as isolation or bedrest studies). However, the experience gained from the initial approach seems promising. Some findings are of special interest. We did not find a linear relation between P300 occurrence and better performance, but an inverted V-shaped relation to difficulty with respective performance differences. Thus, smaller P300-amplitudes with either easy or very difficult conditions were found.

We could also not significantly verify a tradeoff between the primary and secondary task. Performance in the secondary task was constantly very high and did not vary. Thus, any correlational analysis was obsolete. We concluded that the reason is a ceiling effect of the performance data in this special cohort of well-trained professionals.

Overall, we suggest that P300 is a useful method for gauging an operator's cognitive capacity during mission relevant tasks like the hand-controlled docking of a spacecraft on a space station. Decreased P300 magnitude could be an indicator for a lack of free cognitive capacity, which is needed for unexpected changes or events. Kramer et al.[13] showed that during a simulated aircraft flight scenario the amplitude of P300 decreased with task difficulty, but only in well trained subjects. We propose that training should be continued until individuals demonstrate sufficient cognitive spare capacity by a clear P300 during the training. Thereby, reliability of this operation and mission safety would be enhanced. However, this study generally confirmed the high level of skills of cosmonauts in this very specific operational task—the manual docking maneuver.

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Authors and Affiliations: Juri A. Bubeev, Prof. Dr. med., Tatyana I. Kotrovska, Prof. Dr. med., and Darya Schastlivtseva, Dr. eng., Science State Scientific Center of the Russian Federation, Institute of Biomedical Problems of the Russian Academy of Sciences, Moscow, Russian Federation; Bernd Johannes, Dr. rer. nat., and Hans-Juergen Hoermann, Dr. phil., German Aerospace Center, Cologne, Germany; Sergey Bronnikov, Dr. eng., Rocket and Space Corporation "Energia" S. P. Korolev, Korolev, Moscow Region, Russian Federation; and Anthony W. K. Gaillard, Prof. Dr., Tilburg University, Tilburg, Netherlands.

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Body Bag Cooling with Two Different Water Temperatures for the Treatment of Hyperthermia

Kevin C. Miller; Noshir Y. Amaria

INTRODUCTION: Exertional heatstroke (EHS) is a life-threatening condition that requires quick recognition and cooling for survival. Experts recommend using cooling modalities that reduce rectal temperature (T_{REC}) faster than 0.16°C/min though rates above 0.08°C/min are considered "acceptable." Hyperthermic individuals treated in body bags filled with ice water (~3°C) have excellent cooling rates (0.28 ± 0.09°C/min). However, clinicians may not have access to large amounts of ice or ice water when treating EHS victims. The purpose of this study was to determine if using a body bag filled with water near the upper limits of expert recommendations for EHS treatment would produce acceptable (>0.08°C/min) or "ideal (>0.16°C/min)" T_{REC} cooling rates or different nadir values.

METHODS: A total of 12 individuals (9 men, 3 women; age: 21 ± 2 yr; mass: 74.6 ± 10.2 kg; height: 179.5 ± 9.6 cm) exercised in the heat until T_{REC} was 39.5°C. They lay supine while 211.4 ± 19.5 L of 10°C (Ten) or 15°C (Fifteen) water was poured into a body bag. Subjects cooled until T_{REC} was 38°C. They exited the body bag and rested in the heat for 10 min.

RESULTS: Subjects exercised in similar conditions and for similar durations (Ten = 46.3 ± 8.6 min, Fifteen = 46.2 ± 7.8 min). T_{REC} cooling rates were faster in Ten than Fifteen (Ten = 0.18 ± 0.07°C/min, Fifteen = 0.14 ± 0.09°C/min). T_{REC} nadir was slightly higher in Fifteen (37.3 ± 0.2°C) than Ten (37.1 ± 0.3°C).

DISCUSSION: Body bag cooling rates met expert definitions of acceptable (Fifteen) and ideal (Ten) for EHS treatment. This information is valuable for clinicians who do not have access to or the resources for ice water cooling to treat EHS.

KEYWORDS: exertional heat stroke, Polar Life Pod, portability, rectal temperature.

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Rapid recognition and whole-body cooling is critical to reduce exertional heatstroke (EHS) morbidity and mortality.[2,3,5] Fortunately, many tools are available to perform cold water immersion (CWI) in the field and range from stationary tubs/pools[25] to more portable options like tarp-assisted cooling with oscillation (TACO).[7,11] Having portable CWI methods are important because some of these tools are relatively inexpensive and provide the clinician options to treat EHS in a variety of terrains and locations. Some expert pronouncements[2,14] recommend immersing EHS patients up to the neck in water between 1.7°C and 15°C with the goal being to have "acceptable" or "ideal" cooling rates during treatment (0.08°C/min to 0.15°C/min or >0.16°C/min, respectively).[12]

Recently, Miller and Amaria[13] demonstrated body bag cooling with a device called the Polar Life Pod® (Polar Products, Inc; Stow, OH, United States) was effective at treating exercise-induced hyperthermia. The cooling rates were excellent (0.28 ± 0.09°C/min) when 152 L to 227 L (40 to 60 gal) of ice water (~3°C) were used and similar to those from the stationary tubs frequently used in the field to treat EHS patients.[3,25] Unfortunately, using ice water in the body bag also produced significant rectal temperature (T_{REC}) afterdrop and low T_{REC} nadir.[13] This could potentially lead to overcooling and hypothermia and necessitate rewarming procedures. While experts[2,20] often recommend using ice water when treating EHS, some clinicians may not have access to large amounts of ice or ice water. Moreover, ice water initially prepared and reserved for use in

From the Department of Health and Human Performance, Texas State University, San Marcos, TX, and University Health Service, University of Michigan, Ann Arbor, MI, United States.

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Address correspondence to: Kevin C. Miller, Ph.D., LAT, ATC, Department of Health and Human Performance, Texas State University, San Marcos, TX 78666; kmiller@txstate.edu.

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emergency situations may increase in temperature if exposed to hot and humid environmental conditions over time, thereby reducing the thermal gradient when used to treat an EHS victim.

When hyperthermic humans are immersed in stationary tubs filled with warmer water (10–26°C), authors have observed lower, but still acceptable T_{REC} cooling rates.[16,17,23] However, these authors[16,17,23] used water volumes considerably larger than is possible with body bag cooling. Determining the cooling efficacy of body bags with water temperatures at the high end of expert recommendations[2] is crucial because not all clinicians have access to large volumes of ice or ice water in emergency settings. To our knowledge, no one has examined whether cold or cool water placed in body bags results in cooling rates consistent with EHS survivability.

The purpose of this study was twofold. First, we questioned whether 10°C (Ten) or 15°C (Fifteen) water used in body bags would reduce T_{REC} at "acceptable" or "ideal" rates.[12] Second, we determined if T_{REC} cooling rates differed between water temperatures or had different nadir values. We hypothesized T_{REC} cooling rates and nadir values would differ between water temperatures, be acceptable with Fifteen, and ideal with Ten.

METHODS

A randomized (order of testing), crossover, counterbalanced, repeated measures design guided data collection in this study. The independent variables were water temperature (Ten or Fifteen) and time (factor levels varied according to the dependent variable). We chose Ten and Fifteen for our water temperatures to emulate a situation where a clinician lacked access to large quantities of ice and had to use cold water rather than ice water in the body bag. Ten and Fifteen met this criteria while also still falling within professional recommendations for water temperature for EHS victims.[2]

The dependent variables were T_{REC} cooling rates and T_{REC} nadir. T_{REC} was measured every 5 min during exercise, every 0.5 min during cooling, and every 5 min during recovery. We also measured environmental chamber temperature and relative humidity, pre-exercise hydration status, and exercise duration for consistency between testing days.

Subjects

Sample size was estimated a priori using the following assumptions: an alpha value of 0.05, a difference in cooling rate of 0.10°C/min, 80% power, and a standard deviation of 0.06°C/min. Based on these assumptions, we needed 10 subjects to observe statistically significant differences in cooling rates.

We tested a convenience sample of 13 healthy, physically active, college-age men and women. One subject discontinued testing due to the difficulty of the exercise protocol. A total of 12 subjects completed testing (subject demographics can be found in **Table I**). Individuals were excluded from participating if they self-reported: 1) an injury or illness which impaired their ability to exercise; 2) any neurological, respiratory, gastrointestinal, esophageal, or cardiovascular diseases; 3) taking any medications that may have affected fluid balance or temperature regulation; 4) a sedentary lifestyle (defined as exercising <30 min three times per week)[24]; 5) a history of heat-related illness in the 6 mo preceding data collection; 6) current pregnancy; 7) cold allergy; or 8) positive COVID test result within 14 d of testing days. All women were tested within the follicular phase of their menstrual cycle (i.e., first 14 d after the onset of menstruation) and none of the women reported taking a hormone-based birth control. All subjects signed a written informed consent prior to testing and all procedures were approved by Central Michigan University Institutional Review Board.

Table I. Subject Demographics and Hydration Information.

DEMOGRAPHIC/HYDRATION INFORMATION	TEN	FIFTEEN
Demographics		
Age (yr)	21 ± 2	
Men and women (*N*)	9 and 3	
Body mass index	23 ± 3	
Body fat (%)	11 ± 8	
Body surface area (m^2)	1.93 ± 0.17	
Hydration Indices		
Pre-exercise urine specific gravity	1.006 ± 0.005	1.007 ± 0.006
Body mass pre-exercise (kg)	74.59 ± 10.19	74.55 ± 10.01
Body mass postexercise (kg)	73.66 ± 10.23	73.60 ± 10.02
Sweat rate ($L \cdot h^{-1}$)	1.00 ± 0.19	1.01 ± 0.18
Post-testing hypohydration (%)	1.29 ± 0.36	1.28 ± 0.30

Data are means ± SD, *N* = 12.

Procedures

Procedures for this study were similar to our prior study.[13] Subjects reported for 2 d of testing between 08:00 and 17:00. Subjects were instructed to abstain from exercise (24 h) and stimulants (e.g., caffeine) and depressants (e.g., alcohol) for at least 12 h. They were instructed to drink water regularly throughout the day preceding testing to ensure their urine was clear or light yellow. Compliance with these instructions was self-reported prior to testing.

Approximately 45 min prior to the subjects' arrival, we began filling six 37.8-L (10-gal) water coolers. Due to the specificity of each water temperature in this study, we mixed ice and tap water as necessary until the water in the middle of the cooler was ~9.8°C or ~14.8°C since we anticipated the water would warm slightly while the participant exercised. No ice was visible in the coolers on each day once preparation was completed. Each cooler lid was numbered so we could average the temperatures of the water from the coolers used during treatment in the event we did not use the water from all six coolers for a participant.

Upon participants' arrival, they voided their bladders completely and a spot urine-specific gravity assessed hydration status (SUR-Ne refractometer, Atago USA Inc., Bellevue, WA, United States). If urine specific gravity indicated subjects were hypohydrated (i.e., >1.020),[21] subjects consumed ~1 L of water and urine specific gravity was reassessed ~45 min later. If subjects were still hypohydrated, they were rescheduled. If euhydrated, subjects were weighed nude (Defender #5000, Ohaus Corp, Parsippany, NJ, United States). Then they dressed in undergarments (sports bras also for women), shorts, socks, and t-shirts. We measured skinfolds at the chest, abdomen, and thigh (men) and the triceps brachii, abdomen, and thigh (women) in triplicate per Pollack, Schmidt, and Jackson[19] (baseline skinfold caliper #12-1110, Fabricated Enterprises, Inc, White Plains, NY, United States). Skinfolds were averaged at each site and summed to estimate body density[8] and percent body fat.[22] Body surface area was estimated using Dubois and Dubois's equation.[4]

Subjects donned a heart rate monitor (Polar Electro, Inc, Lake Success, NY, United States) and self-inserted a rectal thermistor (#401, Advanced Industrial Systems; Prospect, KY, United States) 15 cm past the anal sphincter.[15] They entered an environmental chamber and we recorded the environmental temperature and humidity (Kestrel Heat Stress Tracker #4400, Nielsen-Kellerman, Boothwyn, PA, United States). T_{REC} was recorded and they stood on a treadmill for 10 min to acclimate to the heat. Subjects performed an exercise protocol on a treadmill consisting of walking for 3 min at 3 mph and running at approximately 90% of their age-predicted maximum heart rate for 2 min (0% incline). When subjects' T_{REC} reached ∼38.2°C, an assistant stirred the water in each cooler and measured the water temperatures by placing a #401 thermistor approximately halfway (30.5 cm; 12 in) in the center of the cooler. Then, we moved the coolers from our main laboratory (∼22°C) inside the environmental chamber.

Once subjects' T_{REC} reached 39.5°C, they removed their shoes and lay supine inside the body bag (Polar Life Pod®, Polar Products, Inc.; **Fig. 1**). We purposefully used water temperatures at the higher end of the manufacturers[6] and expert recommendations[2] and we did not follow the manufacturer recommendation[6] to add ice or colder water to the body bag if water temperature exceeded 15°C over the course of treatment to test our hypothesis. For shorter subjects, we folded the end of the body bag closest to the subjects' feet to minimize water accumulation at the end of the unit. One investigator poured the prepared water into the body bag so subjects' torso, arms, legs, and neck were covered. Subjects' heads rested on a pillow included with the unit to ensure airway patency during cooling. A separate #401 thermistor was placed next to the subjects' neck into the water so we could monitor the water temperature in the body bag during cooling. The body bag's zipper was closed and the straps were secured. We recorded the volume of water initially added. The body bag was shaken continuously side-to-side during cooling. The body bag water temperature was also monitored and recorded once subjects' T_{REC} reached 38°C.

Fig. 1. A subject being cooled in the Polar Life Pod®.

T_{REC} was recorded every 0.5 min during cooling. A standard stopwatch was started when we began pouring water on top of subjects. The stopwatch was stopped when subjects' T_{REC} reached 38°C. Cooling rates were calculated by taking the difference in body temperatures from the end of exercise to the end of treatment and dividing it by the amount of time necessary to reduce T_{REC} to 38°C.

Subjects self-reported shivering onset during cooling so we could ascertain if shivering-induced thermogenesis affected cooling duration. Once T_{REC} was 38°C, subjects exited the body bag and towel dried their arms and legs. They sat in the environmental chamber for 10 min to recover and we recorded environmental conditions. After recovery, subjects exited the chamber, removed the rectal thermistor, towel dried, were weighed nude a second time, and excused.

No fluids were given to subjects once they entered the environmental chamber. Subjects completed their second testing day at approximately the same time of day (± 3 h) and at least 48 h after the first testing day.

Statistical Analysis

Since exercise and CWI durations differed between subjects, we only statistically compared T_{REC} at times common to all subjects. Means and standard deviations were calculated for each dependent variable and assessed for normality. Separate dependent *t*-tests were used to examine T_{REC} cooling rates, T_{REC} nadir, pre-exercise urine specific gravity, environmental conditions, and exercise durations.

We used repeated measures ANOVA to analyze T_{REC} during exercise, cooling, and recovery between conditions. Sphericity was assessed with Mauchly's test. Geisser-Greenhouse adjustments to *P*-values and degrees of freedom were made if the sphericity condition was violated. Upon significant interactions or main level effects, Tukey-Kramer post hoc tests identified differences between cooling methods at each time point. Significance was accepted when $P < 0.05$ (Number Cruncher Statistical Software v.2007, Kaysville, UT, United States).

RESULTS

All subjects self-reported compliance with testing instructions each day. Subjects were euhydrated before exercise [$t_{(11)} = 0.63$, $P = 0.54$, Table I] and exercised for similar durations [$t_{(11)} = 0.16$, $P = 0.44$, **Table II**]. Environmental chamber temperature [$t_{(11)} = 0.76$, $P = 0.46$] and humidity [$t_{(11)} = 1.1$, $P = 0.30$] were similar between days (Table II).

Table II. Exercise and Cooling Data.

EXERCISE/COOLING	TEN	FIFTEEN
Exercise Conditions		
Exercise duration (min)	46.3 ± 8.6	46.2 ± 7.8
Environment temperature (°C)	36.8 ± 0.2	36.7 ± 0.3
Environment relative humidity (%)	44 ± 1	44 ± 1
Cooling Descriptives		
T_{REC} cooling rate (°C/min) [*]	0.18 ± 0.07	0.14 ± 0.09
Nadir T_{REC} (°C)[*]	37.1 ± 0.3	37.3 ± 0.2
Preimmersion water temperature (°C)[†, ††]	10.03 ± 0.07	14.92 ± 0.04
Postimmersion water temperature (°C)[‡, ††]	13.75 ± 0.95	18.33 ± 0.97
Water volume utilized for cooling (L)[**, ††]	211.4 ± 19.5	211.4 ± 19.5
Subjects who self-reported shivering during or after CWI (*N*)[††]	11	7
Time to shivering onset (min)[††]	6.3 ± 2.7	9.3 ± 4.5

All data are means ± SD (*N* = 12). T_{REC} = rectal temperature. [*] = Significantly different between conditions ($P < 0.05$). [†] = This is the average water temperature in the coolers when T_{REC} was approximately 38.2°C during exercise. [‡] = This is the temperature of the water located near the subject's neck when T_{REC} was 38°C. [**] = These are approximate starting volumes of water used within each condition. Because the body bag was not watertight, some water was lost while attempting to fill it during cooling. [††] = Data reported descriptively and not statistically analyzed.

Subjects' T_{REC} were consistent during exercise each day and everyone discontinued exercise when T_{REC} was 39.5°C (**Fig. 2**, $P > 0.05$). However, T_{REC} cooling rates [$t_{(11)} = 2.0$, $P = 0.03$, Table II] and T_{REC} nadir differed between water temperatures [$t_{(11)} = 2.6$, $P = 0.01$, Fig. 2, Table II].

DISCUSSION

This is the second study we completed examining the effectiveness of body bag cooling as a tool for treating hyperthermia. In our first study,[13] we observed using 202.7 ± 23.8 L of 3.2°C ice water in a body bag quickly cooled subjects (0.28 ± 0.09°C/min). However, our original study presumed clinicians had access to modest quantities of ice (24 gal, 91 L) to achieve ice-water temperatures. In the current study, we intentionally filled the body bag with water at temperatures at the higher end of the manufacturer[6] and professional recommendations[2] to determine if body bag cooling would meet expert[12] recommendations for ideal or acceptable cooling. Our main observation was body bag cooling was still able to meet expert recommendations for ideal cooling with Ten and acceptable cooling with Fifteen.[12] Clinically, this means clinicians who do not have access to large quantities of ice or only have access to cold tap water can still use body bag cooling effectively so long as the water temperatures fall within official recommendations.[2] These results are encouraging because they indicate body bags can be an effective tool for treating hyperthermia, and possibly EHS, even when optimal parameters for its use are not present.

The body bag cooling rates in the current study were comparable to or exceeded the average cooling rates of several other studies examining portable CWI techniques. When authors used 2.1°C and 9°C water with TACO, they observed cooling rates of 0.14°C/min and 0.17°C/min.[7,11] More recently, Klous et al.[10] used 80 L (21 gal) of 27.2°C water and TACO and noted acceptable cooling of 0.12 ± 0.03°C/min. When unknown volumes of ice and water were put in a medical body bag up to a patient's midaxillary line, emergency room physicians observed an oral temperature cooling rate of 0.16°C/min.[9]

We acknowledge our current and prior[13] body bag results are significantly faster than Nye et al.,[18] who observed body bag cooling rates of 0.04 ± 0.08°C/min. The slow cooling rates in their study[18] were likely due to subjects being only mildly hyperthermic (T_{REC} averaged 38.4°C), the potential lack of convective cooling during treatment, and water likely accumulating at the end of the unit due to a failure to adjust the size of the body bag based on subjects' height. Regardless, the current data and those from others[7,9,11] suggest clinicians have several effective portable CWI tools available to treat EHS. Therefore, clinicians should consider athlete size, number of people available to help treat EHS victims, tool cost, and terrain when designing heat illness policy and procedure documents if these portable CWI tools are going to be used to treat EHS.

We believe the differences in cooling rates between portable CWI studies can be explained primarily by experimental differences in water volume and water temperature. Water temperature is one of the primary factors affecting cooling rates of

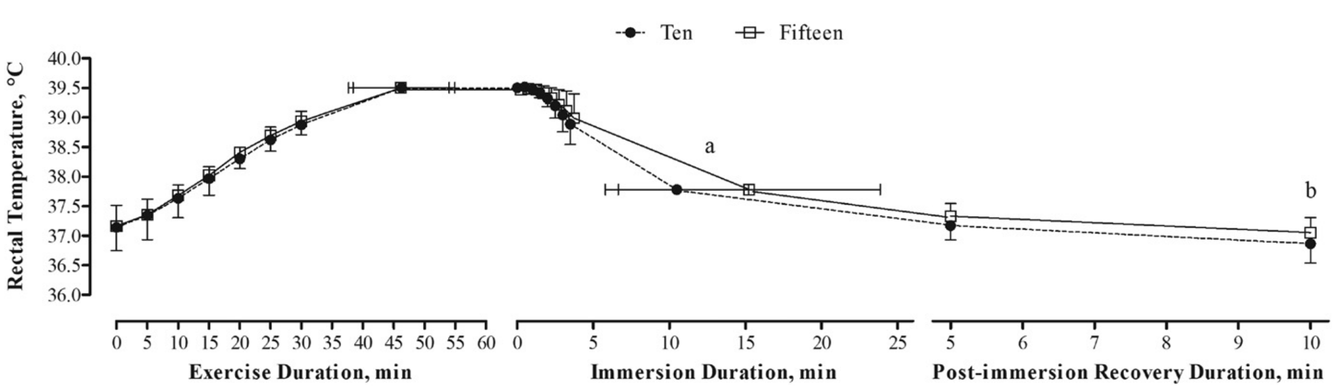

Fig. 2. Body bag cooling with two different water temperatures. Time 0 indicates the start of exercise or cooling. X-axis error bars in exercise duration and immersion duration indicate the SD of the final exercise and CWI durations. [a] = Ten cooling duration < Fifteen cooling duration [$t_{(11)} = 2.7$, $P = 0.01$]. [b] = Ten T_{REC} nadir < Fifteen T_{REC} nadir [$t_{(11)} = 2.6$, $P = 0.01$].

hyperthermic individuals and EHS patients.[20,25] Proulx et al.[20] observed some of the fastest T_{REC} cooling rates reported in the literature when hyperthermic subjects (T_{REC} = 40°C) were immersed up to their clavicles in 2°C water (0.35 ± 0.14°C/min). When warmer water temperatures of 8°C, 14°C, and 20°C were used, cooling rates slowed by 46% (0.19 ± 0.07°C/min), 57% (0.15 ± 0.06°C/min), and 46% (0.19 ± 0.10°C/min), respectively. Similarly, Miller et al.[17] observed an average cooling rate of 0.12 ± 0.05°C/min when subjects were immersed up to the neck in 21°C water. Taylor et al.[23] also observed temperate water (26°C) was capable of cooling subjects within acceptable ranges (0.10 ± 0.02°C/min). In the current study, because we did not replace or add new, colder water or ice during cooling, we observed substantial increases in water temperature within the body bag of 3.72°C (Ten) and 3.42°C (Fifteen) by the time subjects finished cooling. Even with these temperature increases, the body bag was still capable of holding enough cold water to cool at acceptable rates.

Water volume and, in turn, body surface area covered during cooling are two other important factors affecting cooling rates.[1] One advantage of body bags is water can cover the chest and most of the body (minus the face) because they can be closed around the patient. This is advantageous since it ensures greater body surface area coverage. In two of the TACO studies, authors used 30–40 gal (113 L to 151 L) of water to treat hyperthermic subjects. The smaller water volumes and fact that water often accumulates over the torso rather than fully covering the entire body with TACO is one consideration clinicians need to factor in when considering which portable tool to use. Conversely, body bags are able to accommodate about 40% more water while covering the entire body. One concern, however, is water can leak from the bag during treatment, especially from the area around the head. Regardless, having more water is desirable because, as hyperthermic subjects cool, the water inside the body bag will warm and the thermal gradient between the body and water will be reduced, leading to slower cooling rates. This explains the ∼3.5°C increase in water temperatures at the end of cooling in the body bag. We intentionally did not add any new, colder water or ice to the body bag once we began immersion to test the efficacy of the body bag with several constraints. However, if clinicians followed the manufacturer recommendation[6] to add ice or colder water if the water in the body bag exceeded 15°C, it is likely the thermal gradient would be maintained or enhanced and the cooling rates could exceed those reported in this study.

A secondary aim in this study was to determine if T_{REC} nadir could be improved with warmer water to reduce the risk of overcooling and hypothermia. While T_{REC} nadir in Ten and Fifteen were statistically different in this study, the minor difference of 0.2°C is unlikely to be clinically meaningful. However, T_{REC} nadir was ∼0.5°C higher than our first body bag study, which used ice water (∼3°C). Moreover, shivering onset was delayed 3–6 min by using Ten and Fifteen compared to our first study.[13] Consequently, using warmer water in the body bag allowed for less afterdrop and was tolerated much more effectively than ice water. Thus, it is likely fewer rewarming efforts or cold-water shock responses would occur if clinicians use Ten or Fifteen in a body bag.

We acknowledge our study's limitations. First, our subjects likely had normal thermoregulatory capabilities because none of our subjects experienced EHS. This is a common limitation of hyperthermia studies done within the context of a university laboratory setting. Studying the effect of body bag cooling in patients with EHS is necessary in the future to confirm these results. Second, the volume of water poured into the body bag for each participant varied since some water leaked out of the system, mostly near the head and rectal thermometer port, during cooling. Thus, reported immersion volumes must be considered rough estimates. Third, subjects were not immediately immersed in the body bag each day. We estimate it took ∼2 min to pour the water onto subjects, close the zipper, and secure the straps of the body bag device. Finally, we only measured T_{REC} for 10 min post-immersion. It is possible T_{REC} nadir would have been lower had the recovery period been longer. However, the cooling rates from 5 min to 10 min post-immersion in both conditions were <0.03°C/min. Consequently, we do not feel this limitation changes our clinical interpretation of the data.

In conclusion, using Ten or Fifteen in the body bag produced acceptable to ideal T_{REC} cooling rates[12] and reduced T_{REC} afterdrop. Consequently, clinicians with limited access to ice or ice-cold water can still use body bags to treat hyperthermia. However, the fastest cooling rates will occur by following professional recommendations[2] and using the coldest water. Overall, body bags may be another effective tool, like TACO,[7,10,11] for clinicians to consider when developing their heat illness policy and procedures. Future research on the effectiveness of body bags in treating EHS is still required, but these results and those of others[9,13] show promise that body bag cooling could be another life-saving technique to combat EHS mortality.

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Authors and Affiliations: Kevin C. Miller, Ph.D., ATC, Department of Health and Human Performance, Texas State University, San Marcos, TX, United States; and Noshir Y. Amaria, D.O., ATC, University Health Service, University of Michigan, Ann Arbor, MI, United States.

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Screening for Coronary Artery Disease in Asymptomatic Pilots with Diabetes Mellitus

Meryem Zerrik; Amal Moumen; Mouna El Ghazi; Fahd Bennani Smiress; Zakaria Iloughmane; Choukri El M'hadi; Mohamed Chemsi

INTRODUCTION: Coronary artery disease (CAD) is a cause of death in 75% of patients with diabetes. Its often asymptomatic nature delays diagnosis. In aeronautics, it can cause in-flight incapacitation, beyond which it represents a major fear for the medical expert. Screening for CAD is still a topical subject with the advent of new cardiovascular (CV) risk biomarkers and more effective screening tests. We report the experience of the Aeromedical Expertise Center of Rabat in this screening of diabetic pilots, with a recommendations review.

METHODS: A prospective study over 1 yr included diabetic pilots who benefited from systematic screening for CAD after a CV risk stratification. Coronary angiography is performed if a screening test is positive. Subsequent follow-up is carried out in consultation with the attending physician with regular evaluation in our center.

RESULTS: There were 38 pilots included in our study. The average age was 55 ± 4.19 yr and about 73% had a high CV risk. CAD was detected in 4 cases (10.52%) who had abnormal resting electrocardiograms and required revascularization with the placement of active stents. Approximately 75% of pilots with CAD returned to fly through a waiver with restrictions.

DISCUSSION: Screening for coronary disease in diabetics is controversial, and current recommendations are not unanimous. In our study, the screening did not identify coronary diabetic pilots who could benefit from bypass surgery. Nevertheless, coronary disease was diagnosed, justifying grounding to preserve flight safety, which is an absolute priority in aviation medicine.

KEYWORDS: in-flight incapacitation, silent myocardial ischemia, flight safety, coronary artery disease, diabetes mellitus.

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Diabetes mellitus (DM) is one of the fastest growing global health emergencies of the 21st century.[11] An estimated 463 million people are living with DM, a number that has doubled over the past 20–30 yr. Diabetes prevalence has risen faster in low- and middle-income countries than in high-income countries.[18] Stepwise's Moroccan survey observed an increasing prevalence of diabetes from 6.6–10.6% between 2000–2017.[13]

Over time, DM leads to target organ damages with cardiovascular (CV) complications, diabetic retinopathy, nephropathy, and neuropathy. The incidence of CV events is greater in people with diabetes. Diabetes confers a twofold excess risk for coronary heart disease, the main cause of mortality and morbidity in these patients.[7] In aircrew, the Federal Aviation Administration declared that diabetes prevalence in U.S. civil pilots increased from the mid-1990s through 2005 (i.e., 1.57%),[15] thus pilots are not spared from this pandemic and its coronary risk. Unfortunately, in diabetic patients, coronary artery disease (CAD) is often asymptomatic until the onset of an acute coronary event. This event can occur in pilots with diabetes and cause in-flight incapacitation or sudden death. Moreover, the International Air Transport Association found acute coronary syndromes to be the leading cause of sudden incapacitation during either military or civilian flight operations resulting in

From the School of Medicine and Pharmacy, Mohamed V University, Rabat, Morocco.

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Address correspondence to: Dr. Meryem Zerrik, Hay Ryad, Rabat 10100, Morocco; meryemdoc08@gmail.com.

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aircraft accidents and fatalities.[2] Even if silent coronary disease is frequent in patients with diabetes, its detection in primary prevention is still debated.[16]

Several noninvasive screening tools have been proposed to detect CAD, and new screening methods with greater performance are now available. However, their prognosis value, cost-benefit ratio, and the potential harms of such approaches must be carefully evaluated, mainly in aircrew members. This paper aimed to evaluate the efficiency of a systematic silent myocardial ischemia (SMI) screening in asymptomatic diabetic pilots.

METHODS

Subjects

In a retrospective cross-sectional study, we enrolled pilots presenting themselves for a Class 1 medical examination performed in the Aeromedical Expertise Center of the Military Teaching Hospital Mohamed V of Rabat, Morocco, from January 1 to December 31, 2020. We included in the present study all civilian airline pilots having established type 2 diabetes, who performed a periodical visit examination during the period of study. For pilots requiring more than one medical examination during the study period, only their first examination was included in the study. Patients included had to be under antidiabetic therapy, have a waiver for diabetes, and be asymptomatic from any typical or atypical symptoms of CAD. Military pilots were excluded because we aimed to have a homogenous population to evaluate in the present study.

Pilots were informed about the study and agreed to participate, without any objections, to achieve their health benefits and to enhance scientific goals. The Scientific Research Committee of the Mohamed V Military Hospital determined that this study was exempt from Institutional Review Board approval because the goal of the study is to evaluate the efficiency of our screening strategy, as we do for all diabetes aircrew (as described in the Moroccan rules), and they gave permission to publish the results in the national and international communities. An additional consideration was that the population included in the study would have to undergo the same evaluation and the same decision regardless of inclusion in the study, meaning there were no new experiences or examinations required of them specifically for the study.

Materials

Data on patient demographics, medical history, comorbidities, laboratory and vital status measurements, micro- and macrovascular complications, medications, and total flight hours (TFH) were collected from pilots' medical records at the airline's medical center in an anonymous format. In order to assess CV risk factors, anthropometric data and CV risk factors were compiled from participants' medical records.

Hypertension was diagnosed if subjects were on drug treatment for hypertension or had a systolic blood pressure of ≥130 mmHg and/or diastolic blood pressure of ≥80 mmHg. Obesity was diagnosed if the patient had a body mass index $\geq 30\,\mathrm{kg \cdot m^{-2}}$. Smoking was defined as active smoking or smoking cessation of fewer than 3 yr.

Lipid anomalies assessment was based on enzymatic measurement of total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol after 12 h of fasting. Dyslipidemia was defined by total cholesterol $>200\,\mathrm{mg \cdot dL^{-1}}$ ($5.1\,\mathrm{mmol \cdot L^{-1}}$), LDL cholesterol $>160\,\mathrm{mg \cdot dL^{-1}}$ ($4.13\,\mathrm{mmol \cdot L^{-1}}$), and/or HDL cholesterol $<40\,\mathrm{mg \cdot dL^{-1}}$ ($1.03\,\mathrm{mmol \cdot L^{-1}}$) for men and $<50\,\mathrm{mg \cdot dL^{-1}}$ ($1.29\,\mathrm{mmol \cdot L^{-1}}$) for women, and/or triglycerides $>1.5\,\mathrm{g \cdot L^{-1}}$ or use of lipid-lowering drugs.

The assessment of CV risk was based on CV risk categories developed by the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) 2019 recommendations in the guidelines on diabetes, prediabetes, and cardiovascular diseases (CVD).[5] Individuals with DM and CVD or DM with target organ damage, such as proteinuria or kidney failure (estimated glomerular filtration rate [eGFR] $<30\,\mathrm{mL \cdot min^{-1} \cdot 1.73\,m^{-2}}$), are at very high risk (10-yr risk of CVD death >10%). Patients with DM with three or more major risk factors, or with a DM duration of >20 yr, are also at very high risk. Patients with DM duration >10 yr without target organ damage plus any other additional risk factors are at high risk. Young patients (with type 2 DM and aged <50 yr) with DM duration <10 yr without other risk factors are at moderate risk.[5]

Carotid atherosclerosis and lower limb diabetic arteritis were assessed by Doppler ultrasonography. Microalbuminuria was defined as a urine albumin excretion rate of 30–300 mg per 24 h for 24 h of urine collection (or $20\text{–}200\,\mathrm{\mu g \cdot min^{-1}}$ or $30\text{–}300\,\mathrm{\mu g \cdot mg^{-1}}$ creatinine on two of three urine collections). The eGFR was calculated using the "modification of diet in renal disease" equation, and chronic kidney failure was defined by eGFR $<60\,\mathrm{ml \cdot min^{-1} \cdot 1.73\,m^{-2}}$. A detailed neurological exam and a dilated fundus oculi examination were performed on all patients. ST segment and T-wave changes on previous resting electrocardiogram (ECG) were evaluated.

Procedure

Then we proceeded to a systematic screening based on resting ECG, echocardiography, and ECG exercise tests, which were conducted using the Bruce protocol. Patients with a positive treadmill test underwent coronary angiography. Patients with a borderline exercise test underwent a functional test imaging myocardial perfusion scintigraphy (MPS), stress echocardiography, or stress MRI. Functional test imaging was chosen according to cardiologist advice, patient preference, and test availability in our center.

Statistical Analysis

Statistical analysis was performed with SPSS 18 software. The number of patients and the corresponding percentages were given for categorical variables, mean ± SD was reported to describe the normally distributed continuous variables, and medians with interquartile ranges were reported for continuous variables with skewed distributions. The Kolmogorov-Smirnov test was performed on all measures to assess data normality. Chi-square or Fisher's exact test was used to compare the categorical variables as appropriate. Means were compared using the Student's *t*-test and medians were compared using the Mann-Whitney test. A *P*-value <0.05 was considered statistically significant.

RESULTS

A total of 38 diabetic pilots were eligible for CAD screening in this study. The age distribution ranged from 46–62 yr old, with a mean (SD) of 55 (±4.19) years. All were men, with a median flight time of 6785 h. Diabetes duration varied between 8–13 yr, averaging 8 yr (±4.1). Patients were treated with metformin or dipeptidyl peptidase-4 (DPP-4) inhibitors, or a combination of these two therapies. The average HbA1c was 6.76% (50 mmol · mol^{-1}) (±0.7). Degenerative complications were established: two patients had asymptomatic carotid atherosclerosis in supra-aortic trunk ultrasonography; two patients had microalbuminuria; one case of asymptomatic atherosclerosis in the lower limb arteries; and one case of diabetic retinopathy. The CV risk factors characteristic of diabetic pilots are presented in **Fig. 1**. Hyperlipidemia with or without treatment was present in 42.9% of cases, which was the most represented CV risk factor, and 5.26% of cases presented microalbuminuria, which was the least represented factor. We did not have any cases of associated comorbidities or disorders like obstructive sleep apnea syndrome, nonalcoholic fatty liver disease, or erectile dysfunction. Concerning the CV risk stratification according to the ESC/EAS 2019 recommendations, 74% of our pilots were at a high risk, 21% were at a very high risk, and only 5% were at a moderate risk.

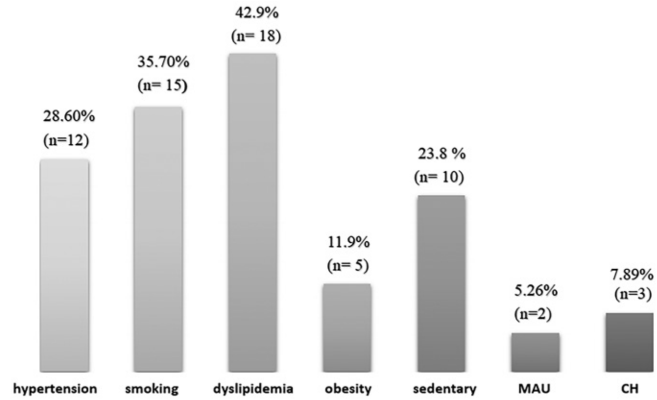

Fig. 1. Cardiovascular risk factors among the studied population out of gender and age. CH = coronary heredity; MAU = microalbuminuria.

An algorithm illustrating the result of the cardiac investigations of our pilots is presented in **Fig. 2**. There were four abnormal resting ECG results observed in the diabetes pilot group (10.52%). T-wave abnormalities were present in two pilots, ventricular extrasystoles were present in one pilot, and left ventricular hypertrophy by voltage criteria was present in one pilot. The ECGs were all normal and all pilots performed exercise stress ECGs. These tests were negative in 32 cases and those patients did not undergo any further testing.

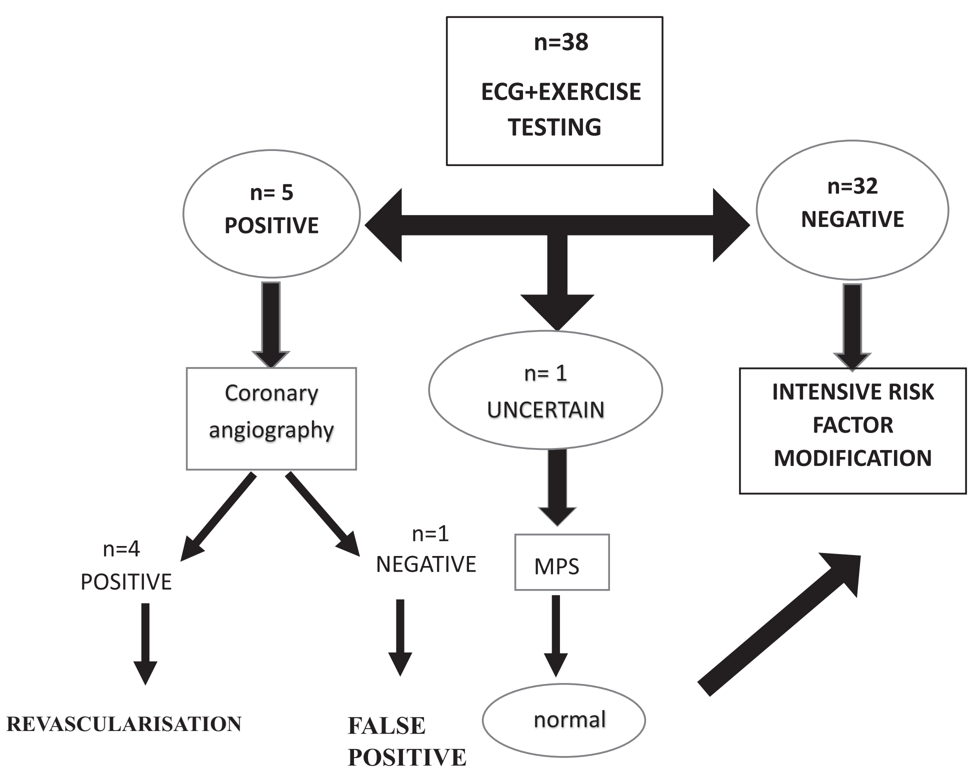

Fig. 2. Algorithm illustrating the result of the screening process.

In five cases, the exercise stress ECG was judged to be positive. In four patients, the ECG showed 1–2.5 mm ST-segment depression, and these patients were referred for coronary angiography. One pilot was found to have severe circumflex branch stenosis, three pilots had anterior interventricular branch stenosis, and one pilot had normal coronary arteries. One pilot presented with borderline ECG results that showed <1-mm ST segment depression and was referred for an MPS, which was normal and showed no myocardial perfusion defect. This patient was not then referred for coronary angiography.

We found four patients who had significant lesions, characterized by more than 70% artery stenosis, and these patients underwent successful percutaneous coronary intervention. Three pilots with CAD returned to flight through a waiver, two pilots after 6 mo and 1 pilot after 1 yr, with some restrictions: there must be a second pilot on-board and they must have a follow up examination every 3 mo. One pilot was declared definitively unfit for Class 1 certification. **Table I** describes the comparison of epidemiological aspects and CV risk factors among subjects with and without SMI.

DISCUSSION

For the first time in our aeromedical expertise center, a systematic screening of SMI was applied to commercial pilots with diabetes and asymptomatic from any typical or atypical symptoms of CAD. For diabetic patients, there are 12 prediction models specifically designed to calculate future CV risk. The risk-prediction model used in this study is the set of CV risk categories according to ESC/EAS 2019 recommendations. The advantage of the model used in this paper is that it requires data to be routinely established at each medical examination.

During recent decades, the risk of CV events has markedly decreased in patients with diabetes through multifaceted improvements in diabetes care, risk factor management, self-management education and support, and better integration of care.[9] However, this risk remains higher than in the general population. CV risk associated with diabetes is heterogeneous.

The prevalence of SMI in randomized clinical trials varies between 5.6–21.1%, depending on the screening strategy.[4] In our study of 38 screened pilots, 4 of them had an SMI, resulting in a prevalence of 10.52%. This exceeded the 1% rule, which is the risk threshold applied to the medical fitness of pilots.

Table I. Comparison of Epidemiological Aspects and Cardiovascular Risk Factors Between Subjects With and Without Silent Myocardial Ischemia.

PILOTS	SMI (*N* = 4)	NO SMI (*N* = 34)	*P*
Age	55.00	55.53	0.813
HbgA1c	7.02%	6.73%	0.44
BMI	26.89	26.79	0.93
Hypertension	25% (*N* = 1)	32.4% (*N* = 11)	1
Dyslipidemia	50% (*N* = 2)	47.1% (*N* = 16)	1
Smoking	75% (*N* = 3)	25.3% (*N* = 12)	0.28
Sedentary	50% (*N* = 2)	23.5% (*N* = 8)	0.27
Family History of CHD	100 (*N* = 4)	52.9% (*N* = 18)	0.12
Obesity	25% (*N* = 1)	11.8% (*N* = 4)	0.44

BMI = body mass index; CHD = coronary heart disease; SMI = silent myocardial ischemia

Even if silent coronary disease is frequent in patients with diabetes, its detection in primary prevention is still debated. Up to 50% of SMI cases are not detected at the time of onset but are instead detected later during routine care when CV symptoms occur, or by cardiac imaging.

Indeed, regarding the screening of asymptomatic patients, the recommendations of several societies are not unanimous. The latest French guidelines, published in 2004, limited the assessment of myocardial ischemia to selected patients.[14] The American Diabetes Association guidelines, released in 2022, recommend not screening asymptomatic diabetes patients for silent CAD, because it does not improve outcomes as long as atherosclerotic CVD risk factors are treated.[1] A risk stratification approach has recently been developed by the European Society of Cardiology in collaboration with the European Association for the Study of Diabetes.[5] This approach starts with a risk stratification that includes: age, type, and duration of diabetes; the number of associated risk factors; and target organ damage. Indeed, carotid or limb arterial ultrasound study, coronary artery calcium (CAC) score, and coronary computed tomography angiography (CCTA) can be used to better assess CV risk. Recently, the French Society of Cardiology and the French-speaking Society of Diabetology proposed a consensus strategy defined by diabetologists, cardiologists, and CV imagers in order to more precisely evaluate coronary risk and propose an algorithm for screening according to risk levels in asymptomatic diabetes patients in primary prevention.

Obviously, aircrew represent a particular group among high-CVD-risk individuals. In addition to common life strain and on-duty factors like hypobaria, pressurization, sedentariness, jet lag, high-caloric foods, etc., aircrew face typical stress such as repeated proficiency simulator checks, intermittent medical exams and total flight hours obligations, employer pressure, responsibility, and scheduled accomplishment. These factors may lead to CVD, either directly or indirectly. They interact with traditional risk factors, behavioral risk factors, and emerging CV risk factors.[3]

The Moroccan aeromedical standards refer to the Equipment and Transport Administration Order No. 1209-09, relating to aircrew members' physical and mental fitness conditions, the accreditation of centers of expertise in aeronautical medicine, and the appointment of medical examiners. They suggest using the treadmill test, MPS, stress echocardiogram, and possible coronary angiography if an asymptomatic CAD is suspected during the aeromedical examination. Furthermore, the 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes recommend (for medicolegal reasons) screening for CAD in asymptomatic subjects whose occupations involve public safety (e.g., airline pilots, or lorry or bus drivers), who must also commonly undergo periodic testing for the assessment of exercise capacity and evaluation of possible heart disease, including CAD.[12] In 2019, the NATO Cardiology Working Group published a consensus for screening and investigation of aircrew for asymptomatic coronary disease, based on a three-phase approach beginning with initial risk stratification using a population-appropriate risk calculator that includes family history and nonfatal and fatal endpoints, like the Reynolds risk equation and a resting ECG. Enhanced screening is recommended for aircrew identified as being at increased risk, by means of CAC Score alone or combined with a CCTA. Additional screening may include exercise testing and vascular ultrasound imaging. Aircrew identified as being at high risk based on enhanced screening require secondary investigations, which may include functional ischemia testing and potentially invasive coronary angiography. Functional stress testing as a stand-alone investigation for significant CAD in aircrew is not recommended.[8]

Exercise stress tests are limited in detecting potentially flow-limiting CAD and predicting future CV events.[17] Despite its low sensibility and specificity in screening for atherosclerosis, exercise test ECG has detected 4 pilots with SMI in our study of 38 pilots with diabetes, which amounts to a prevalence of 10%, with 1 pilot definitively unfit for a Class 1 certification. Exercise stress test remains simple; it has a low cost and is widely available in our center. That's why we chose to include it in our screening strategy. However, it is overtaken by CCTA and CACs, which are more recommended in aircrew with increased risk of CAD; unfortunately, neither test was used in our study due to being both expensive and not yet included in our current national aeromedical recommendations.

CAC score is a rapid, safe, and inexpensive method for detecting coronary atherosclerosis. It is associated with low radiation. The CAC score assesses the volume of coronary calcifications and assumes that each calcification corresponds to an atherosclerotic plaque. Patients are stratified according to the Agatston Score.[6] CAC score has a higher sensitivity and specificity with a positive predictive value for detecting severe lesions (>70%). Nevertheless, the prevalence of a high CAC score is >20% among asymptomatic patients with diabetes, greater than in the elderly and in those without diabetes.[10]

Unlike CACS, CCTA provides information about luminal stenosis's number, extent, and location. It additionally has the advantage of imaging and characterizing plaque (into calcified, noncalcified, or mixed plaque morphology). In asymptomatic patients with diabetes, anatomical analysis of plaques can help to detect future vulnerable plaques at risk of acute future events.[10] Most coronary events that occur in younger individuals are caused by the rupture of non-flow-limiting coronary plaques or superficial erosion-remodeled plaques. However, CCTA is more radiant (2–4 MSV) and has some limitations in the case of obesity or kidney failure. In addition, when the CAC score is high, CCTA analysis becomes difficult due to the blooming effect linked to the presence of calcifications and may overestimate luminal encroachment in CACs of >1000.[5,8]

A cardiac computed tomography protocol that provides CCTA and CACS information may be the preferred modality for aircrew identified as being at increased risk based on enhanced screening. The presence of an obstructive lesion greater than 50% is a reasonable aeromedical threshold for grounding and further investigation.[8]

Finally, the results of our study could be different if we had a larger sample size, including military pilots with diabetes who had specific constraints that could increase CV risk. The results would also be more effective if we had used a more efficient test like CCTA in our screening strategy, which is not widely available in our center.

Despite advances in prevention and early disease intervention, CAD is still the most incapacitating cause in military or civilian aviation, resulting in aircraft accidents and fatalities. DM is a major risk factor for the development of CAD and the aircrew population with diabetes is growing in number worldwide. Many CV risk scores are available that can be applied to patients with type 2 diabetes, but the validity and transportability of such a model to assess aircrew may need to be evaluated in future studies.

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Authors and Affiliations: Asst. Prof. Meryem Zerrik, M.D., Aeromedical Expertise Center, Mouna El Ghazi, M.D., Aeromedical Expertise Center, Fahd Bennani Smiress, M.D., Aeromedical Expertise Center, Asst. Prof. Zakaria Iloughmane, Aeromedical Expertise Center, Asst. Prof. Choukri El M'hadi, Medical Oncology Department, and Prof. Chemsi Mohammed, Aeromedical Expertise Center, Military Mohamed V Teaching Hospital, Rabat, Morocco; and Asst. Prof. Amal Moumen, Endocrinology Department, Moulay Ismail Military Hospital of Meknes, Meknes, Morocco.

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Sleep Inertia in Aviation

Fabien Sauvet; Vincent Beauchamps; Philippe Cabon

INTRODUCTION: Sleep inertia is the transition state during which alertness and cognitive performance are temporarily impaired after awakening. Magnitude and time course of sleep inertia are characterized by high individual variability with large differences between the cognitive functions affected. This period of impairment is of concern to pilots, who take sleep or nap periods during on-call work hours or in-flight rest, then need to perform safety-critical tasks soon after waking. This review analyzes literature related to sleep inertia and countermeasures applicable for aviation.

METHODS: The large part of scientific literature that focuses on sleep inertia is based on studies in patients with chronic sleep inertia. We analyzed 8 narrative reviews and 64 papers related to acute sleep inertia in healthy subjects.

DISCUSSION: Sleep inertia is a multifactorial, complex process, and many different protocols have been conducted, with a low number of subjects, in noncontrolled laboratory designs, with questionnaires or cognitive tests that have not been replicated. Evidence suggests that waking after sleep loss, or from deeper stages of sleep, can exacerbate sleep inertia through complex interactions between awakening and sleep-promoting brain structures. Nevertheless, no meta-analyses are possible and extrapolation to pilots' performances is hypothetical. Studies in real life or simulated operational situations must be conducted to improve the description of the impact of sleep inertia and kinetics on pilots' performances. Taking rest or sleep time remains the main method for pilots to fight against fatigue and related decreases in performance. We propose proactive strategies to mitigate sleep inertia and improve alertness.

KEYWORDS: sleep inertia, strategies, pilot, cognitive performance.

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Fatigue in aviation is defined as "a physiological state of reduced mental or physical performance capability resulting from sleep loss or extended wakefulness, circadian phase, or workload (mental and/or physical activity) that can impair a crew member's alertness and ability to safely operate an aircraft or perform safety-related duties."[30] Fatigue is an important safety risk to civil and military aviation. In addition to acutely decreasing performance in flight, chronic fatigue has negative long-term health effects. Despite flight and duty time regulations and enabling optimal rostering, fatigue cannot be fully suppressed.[65]

In-flight sleep is a widely used countermeasure for sleepiness and impaired performance caused by sleep loss and circadian pressure.[21,24] There are two types of in-flight rests: controlled rest period in the flight deck (basic crew) and rest periods in rest areas (augmented crew with flight duty extension). Controlled rest period occurs when a pilot, who is part of a two-pilot operating crew, is temporarily relieved of operational duties and follows a company "controlled rest procedure" for taking a period of rest and sleep in-seat on the flight deck. Controlled rest taken in the flight deck is different from augmented crew flights, where rest periods are taken in the cabin or bunk and used to extend flight and duty time. This situation increases the sleep duration and the risk of sleep inertia that could impair cognitive performance. This situation could affect the pilots' capabilities, particularly if the wake-up is not scheduled and requires a decision or action within the next minutes after awakening. In this situation, the detrimental effect of sleep inertia could alter flight safety.

Sleep inertia is the period of impaired cognitive performance and grogginess experienced after waking. This period of impairment is of concern to pilots and workers who are on-call,

From the Institut de recherche biomédicale des armées, Brétigny sur Orge, and URP 7330 VIFASOM (Vigilance, Fatigue, et Sommeil), Université de Paris, Université Gustave Eiffel, LaPEA, and Welbees, Paris, France.

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Address correspondence to: Fabien Sauvet, IRBA BP 73, 91220 Brétigny sur Orge, France; fabien.sauvet@gmail.com.

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or who nap during work hours, and need to perform safety-critical tasks soon after waking.

The aim of this review is to analyze the scientific literature related to sleep inertia for aircraft pilots and to propose some validated countermeasures to mitigate the potentially induced cognitive impairments. Investigating proactive strategies for optimal sleep length and timing to minimize sleep inertia and maximize alertness is important for informing guidelines on rest breaks and shift scheduling.

METHODS

Three electronic databases (PubMed, Science Direct, and Scopus) were searched between September 2022 and May 2024 for the search terms paired with "sleep inertia". We removed studies in animal models, without experimental data, and with chronic evaluation of inertia associated with nonrestorative sleep. Moreover, aircraft pilots are fit to fly, therefore we will not deal with sleep inertia associated with a sleep pathology. Ultimately, we analyzed the 8 remaining narrative reviews and 64 experimental studies conducted in healthy subjects and related to acute sleep inertia (**Fig. 1**). The larger part of the studies were conducted in laboratory settings ($N = 58$). A small number ($N = 8$) of studies were conducted vs. a control group (counterbalanced in a crossover design), taking into account the circadian rhythm of performance. Many studies are longitudinal studies (before vs. after sleep comparison). The number of subjects is low (mean = 14 ± 2). Due to the amount of diversity and heterogeneity across studies, conducting a meta-analysis was not appropriate. Indeed, studies differ with regard to the sleep time, the kinetics of cognitive measurements (many studies assess only one point of measurement), the parameters analyzed (subjective or objective parameter, etc.), the delay between wake up and the first measurement, the time of the day, the procedure of awakening (spontaneous or induced, etc.), and the previous sleep debt. Finally, a larger number of publications show designs that have not been replicated, thus decreasing possible comparisons with other studies. Therefore, the published results could not be considered as robust and replicated in ecological situations.

DISCUSSION

Sleep inertia is a paradoxical phenomenon of "waking up tired": a period of impaired cognitive performance and grogginess experienced after waking, which dissipates as time awake increases.[25] The exact function of sleep inertia remains largely unknown. From an evolutionary perspective, it can be assumed that the ability to rapidly awaken from sleep would be advantageous (for example, when awakening in response to a potential threat). A more gradual awakening, however, may also be protective given the complexity of neural circuitry in transitioning from one state to another, as it is discussed in the neurophysiology section below. Sleep inertia may, therefore, be an adaptive mechanism to promote sleep upon awakening so that sleep is maintained when the awakening is undesired. For example, as with the timing of the circadian nadir, sleep inertia may help to maintain sleep in the last part of a nocturnal sleep episode when homeostatic sleep pressure has largely dissipated. Sleep inertia has been added to the Bordely's two-process model of sleep regulation in order to improve the understanding of experimental study observations.[8,19]

Sleep inertia is a challenge for workers who need to perform safety-critical tasks, make important decisions, or operate a

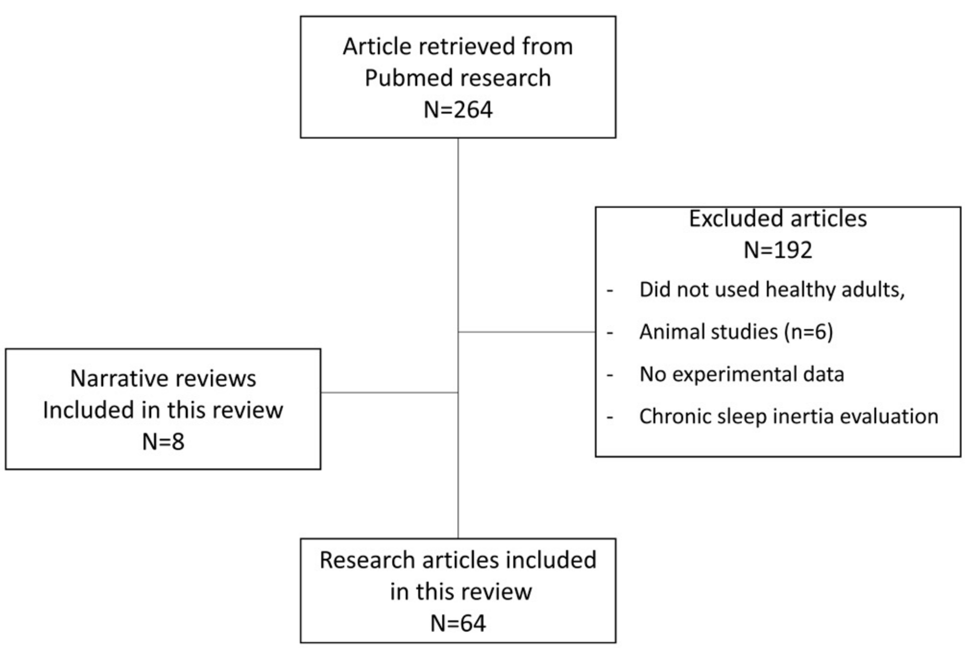

Fig. 1. Flow chart illustrating the structured narrative review selection process for the article population.

vehicle soon after waking. To this end, several reviews of alertness management in operational settings have highlighted the need to manage sleep inertia in order to maintain safety.[10,27,42] Despite its relatively short-acting effects, sleep inertia is a notable cause of performance impairment[62] and has been associated with severe, real-world consequences. In particular, sleep inertia has been a contributing factor in several major accidents and incidents.[38,43,59] For example, an air crash involving fatalities resulted from poor decisions made by the captain, who had just broken from an in-flight nap.[4] Sleep inertia has also been cited as a contributing factor in several commercial incidents across multiple industries which have resulted in damage, injuries, and deaths. Nevertheless, no epidemiological studies related to the frequencies of sleep inertia and/or consequences were found. This might be explained by the fact that in most cases it is difficult or impossible in the accident investigation to determine if the crew was sleeping just before the accident and, therefore, if they were experiencing sleep inertia at the time of the incident or accident.

As sleep inertia literature expands, a debate has begun as to whether all cognitive tasks are equally affected immediately after waking. Some studies have found that, in contrast to the impairment observed after sleep deprivation, only the reaction time or "speed" component of tasks is negatively affected during sleep inertia.[51] However, several other studies have found equal effects on both speed and accuracy, or greater effects on accuracy.[18,54] Variations between studies such as the type of task, time of testing, instructions to the participants (e.g., instructed to perform as fast and/or as accurately as possible), and the length and timing of sleep may explain these discrepancies. Given the range of methodologies used across these studies, a clear hypothesis for the differential effects observed across tasks has yet to be put forward.

Two laboratory studies[29,41] have also claimed that, while overall average response speed may slow down as a result of sleep inertia, lapses, which represent a substantial delay in response speed, are not a neurobehavioral feature of sleep inertia, but rather are only associated with microsleeps induced by sleep loss. In a recent study, Bhatt et al.[7] confirmed that after a 30 min nap, sleep inertia was found to affect the speed component of the task rather than the accuracy in a post-nap period of 30 min. The effect was significant at 6 min following awakening, and after that, the effects dissipated. Nevertheless, sleep inertia is associated with objective changes in brain perfusion or metabolism and could be linked to cerebral responses to sleep pressure.[6] This study suggests that the prefrontal cortex tends to be the longer exposed to sleep inertia compared to the other brain areas.

It has also been argued that higher cognitive tasks that require greater attentional load are more susceptible to the effects of sleep inertia than simple tasks.[10,42] Indeed, studies have reported the effects of sleep inertia on complex cognitive performance tasks such as memory,[1,2] calculations,[10] decision-making[27] and a spatial-configuration visual search task.[10]

While some facets of cognition may be more affected by sleep inertia than others, real-world tasks often involve a combination of multiple cognitive domains. For example, operating a vehicle safely requires situational awareness, information processing, decision-making, memory, and, in some instances, rapid response times. Taken together, the studies' findings suggest that the effects of sleep inertia on simple and complex tasks have the potential to negatively impact safety-critical activities in the real world. Comparison with emergency services activities could be pertinent for the safety implication of fatigue and sleep inertia.[14] However, no study describes examples of medical errors due to sleep inertia. The effects of sleep inertia are still suspected with large references to aviation crash.[4,38,43] Examples of rare immersive or real-life operational design are pertinent for the identification of consequences of sleep inertia in piloting activities. In a more ecological situation, such as a realistic military-type exercise assessing unexpected, abrupt, early-morning awakening effects on immediate "executive function" and the ability to comprehend and deal with a sudden emergency, under a changing situation, after less than 3 h of sleep was studied. A larger part of the groups failed to succeed the tactical change scenario due to many potential factors (social interaction, creativity, etc.).[27]

Different measurements of cognitive efficiency have been identified as crucial to piloting skills, for instance: time-sharing,[60] speed of processing,[56] attention,[33] and problem-solving.[63] One of the most promising approaches consists of administering a test battery to pilots, such as Cogscreen-AE[28] or the Multiple Attribute Task Battery,[13] and correlating their score with their performance during flight simulator sessions or in real flight conditions. Taylor and colleagues[55] were able to predict 45% of the variance of the flight simulator performance with four Cogscreen-AE predictors (speed/working memory, visual associative memory, motor coordination and tracking) in a cohort of 100 aviators (aged 50–69 yr). The main tasks that a pilot must consider could be sorted into four groups: flying, navigating, communicating, and system management. Today, we need more studies to describe the effects or kinetics of sleep inertia on these tasks.

The majority of studies examining sleep inertia were not designed to directly assess the duration of sleep inertia and, therefore, include too few data points to make firm conclusions about the impact of contributing factors on the duration of sleep inertia. In addition, most studies directly observing the time course of sleep inertia have not directly compared contributing factors (sleep debt, hours, etc.). Studies comparing performance after sleep inertia to pre-sleep values have typically shown a return to these levels within 30 min of awakening[9,50,58] and sometimes as soon as 15 min after awakening. Studies that have systematically measured alertness and performance across the period after waking, however, report an asymptotic dissipation of sleep inertia. While the initial dissipation of impairment is rapid, full recovery does not appear to be complete until at least 1 hr after awakening.[2] Jewett et al.[31] found that the impairment is most severe immediately upon waking and then dissipates, generally returning to baseline levels within 15–60 min. These kinetics have been observed in laboratory designs with questionnaires and cognitive tests. There is a lack of observation in operational aeronautical situations or critically stressful contexts.

Time course of sleep inertia is a constant routine protocol in which measurements of subjective alertness and cognitive performance are made regularly from 1 min to 4 hr after scheduled awakening. Under these conditions, Jewett et al.[31] found that subjective alertness continued to improve for up to 2 hr after awakening. Performance impairment on an additional task, however, took up to 3.5 h to dissipate.[31] These tests were performed following a usual morning awakening, so the influence of the rise in circadian alertness across this period cannot be isolated from this observation.

Interestingly, subjective alertness recovered faster than objective performance in the Jewett et al. study but was slower in the Achermann et al.[2] study. They also reported that there was no correlation between objective performance and subjective sleepiness. The difference in time course of performance measures between both studies may be explained by differences in the tasks performed. However, the dissociation of time course between subjective and objective measures in both studies highlights a concern when using self-assessment after waking, especially if subjective alertness recovers faster than cognitive performance.

Subjective ratings of alertness and performance have been shown to be inconsistent predictors of objective performance under conditions of partial and chronic sleep loss. Achermann et al.[2] suggests that subjective ratings might also be a poor indicator of performance across the dissipation of sleep inertia. Hilditch et al. reported a self-rating scale of performance (as opposed to alertness) across the dissipation of sleep inertia and found that despite worse objective attentional performance after waking from a 30-min nighttime nap compared to prenap, participants rated their performance as significantly better during this period.[24] Taken together, these findings highlight the need to measure objective outcomes and/or pilots' performances when investigating sleep inertia effects.

Some factors may positively or negatively influence the degree of sleep inertia. Difficulty getting up is mainly observed after a usual night's sleep. Sleep inertia almost every morning is reported by 42% of adolescents,[3] although confusion on awakening lessens with age in adulthood.[44]

The decrements in performance observed during sleep inertia are exacerbated by prior sleep loss.[24,25] In studies comparing sleep inertia following an 8-h sleep opportunity to partial sleep deprivation, performance upon waking was significantly worse after the partial sleep deprivation night.[41,54] Extended wakefulness prior to a recovery sleep episode can also exacerbate the sleep inertia observed following recovery sleep.[15,48] Dinges et al.[15] observed that after a 2-h nap that followed varying durations of prior wakefulness (6, 18, 30, 42, and 54 h), reaction times slowed down and the number of correct subtractions decreased as time awake prior to the nap increased. In a within-subjects design, Rosa et al.[48] also measured performance after a 2-h nap opportunity following either 16 h of wakefulness or up to 64 h of wakefulness, with worse performance observed after waking from the nap following 64 h. Furthermore, compared to naps taken on daytime flights, naps taken on overnight flights were associated with a significantly higher percentage of deep sleep (11.6% vs. 4.3%).[49]

Sleep inertia is also worsened by cumulative sleep loss. Balkin and Badia's[5] observation of increased sleep inertia effects across 4 nights of disrupted sleep was supported by a recent laboratory study in which participants were studied under conditions of chronic sleep restriction (equivalent to sleep opportunities of 5.6 h per 24-h day).[40] Notably, compared to a control condition (equivalent to sleep opportunities of 8 h per 24-h day), participants undergoing chronic sleep restriction experienced a 10% worsening of performance immediately upon awakening, with average levels of performance failing to reach baseline levels at 70 min post-awakening. Together, these studies suggest that sleep loss, in the form of restricted sleep, extended wakefulness, or cumulative sleep loss, contributes to increased sleep inertia effects.

Sleep inertia effects are greatest during the biological night, near the circadian low in core body temperature. Using a protocol designed to spread behaviors evenly across all hours of the 24-h day (i.e., forced desynchrony protocol), Scheer et al.[52] found that circadian rhythms significantly influenced the number of correct responses on an additional task performed within 2 min of waking. In this study, circadian effects were greater than sleep inertia immediately after waking. Moreover, Achermann et al.'s[2] study observed that the time course of sleep inertia following an 8-h nocturnal sleep episode and a 2-h evening nap was the same, suggesting that circadian timing and sleep duration under these conditions did not impact duration.

This interaction between sleep loss, circadian timing, and performance during sleep inertia has also been found under conditions of chronic sleep restriction.[15] The results of these studies suggest that circadian rhythms have a direct effect on sleep inertia and also moderate the effects of sleep deprivation. This interaction creates a nonlinear trend in performance as sleep deprivation increases. Furthermore, it has been suggested that a participant's morning or evening preference (chronotype) should also be measured when estimating the time course of sleep inertia, with the observation that later chronotypes took longer to recover from sleep inertia than early types,[47] suggesting an individual variability in sleep inertia effects.

Studies showed mixed results regarding the onset of slow-wave sleep (SWS) and the duration and severity of sleep inertia following short naps, making guidelines regarding their use unclear. The varying results are likely due to differing sleep/wake profiles before the nap of interest and the time of the day at waking.[18,24] Mixed observations have been reported on whether the depth of sleep or the stage of sleep at awakening has a significant effect on sleep inertia. The increased amount of, and greater propensity to wake from SWS under conditions of, sleep pressure may be associated with the observed increase in sleep inertia following sleep loss. Similarly, the observation that sleep inertia is less likely to occur after short naps (≤30 min) may be due to the typical latency in SWS onset of 30 min.[9,24,58] However, Dinges et al.'s[15] study of 2-h naps during 54 h of sleep deprivation observed that SWS during the preceding nap was associated with worse performance on a subtraction task immediately after awaking. Several other studies have also observed the sleep stage at awakening as a key predictor of performance impairment upon waking. Stampi[53] reported that participants waking from SWS showed a 41% reduction in performance upon awakening compared to performance pre-nap, whereas participants waking from Stage 2 (N2) sleep showed similar performance to those who were already awake.

Overall, it is difficult to draw a clear conclusion as to the role of SWS in sleep inertia. Different study designs and measures of sleep depth make it difficult to compare between studies. However, the current literature suggests that the lengths of prior wakefulness and prior sleep may influence the association between sleep depth and sleep inertia. Moreover, interindividual differences in subjective sleepiness due to sleep inertia is highly stable within individuals after both baseline and recovery sleep periods.[37] From this literature review, we designed a short questionnaire (**Table I**) in order to assess this risk before taking a sleep or nap period. Each "Yes" answer has been associated with sleep inertia in the literature.

Managing the factors influencing sleep inertia can help to support proactive strategies for managing sleep inertia. Many publications recommend naps of 30 min or less to prevent sleep inertia. However, the evidence to support this advice is yet to be thoroughly reviewed. Although the literature on short afternoon naps is relatively comprehensive, there are very few studies on naps of 30 min or less at night.[24,25] Similarly, the observation that sleep inertia is less likely to occur after short naps (≤30 mins) may be due to the typical latency in SWS onset of 30 min.[20,24,58]

However, the duration of the nap is associated with cognitive efficiency. Brooks and Lack[9] compared four different short, afternoon nap lengths and found that while a 10-min nap resulted in immediate performance improvements, a 30-min nap did not provide improvements until 35 min or up to 95 mins after waking, depending on the task. This suggests that the duration of sleep inertia is dependent on both length of nap and type of task. Comparing across studies, Hilditch et al.[24] found that both a 10-min and 30-min nap terminated at 04:00 following acute sleep loss provided no improvements to performance throughout the sleep inertia testing period (up to 60 min,) nor across the remainder of the night (up to 2.5 h). Taken together, these studies suggest that circadian timing and prior sleep-wake history influence sleep inertia duration as well as severity, although the relative influence of these factors cannot be determined from these observations.

Table I. Proposition of Short Questionnaire for Sleep Inertia Risk Evaluation.

QUESTIONS	YES	NO
I have sleep disorders.		
I have chronic diurnal sleepiness (Epworth sleepiness scale >10).		
I always experienced sleep inertia.		
I am in sleep debt.		
The sleep period duration is more than 30 min.		
The sleep period occurs during the physiological night.		
I can't schedule or anticipate my wake-up time.		
I don't use a progressive awakening alarm (light or sound).		

Pilots are considered fit to fly, without chronic daytime sleepiness. Nevertheless, it is advisable to evaluate during medical check the diurnal excessive sleepiness, using an Epworth Sleepiness Scale,[32] and to treat the pathologies or sleep disorders that will be major factors favoring sleep inertia upon awakening.

Use of caffeine is the most effective proactive countermeasure to sleep inertia. When taken before a short nap (e.g., 20 mins), caffeine has been shown to alleviate the symptoms of sleep inertia following the nap.[54,61] However, there are several limitations to the effectiveness and application of this countermeasure in a reactive scenario. When administered after sleep, even in a rapidly absorbed chewing gum format, the effects of caffeine are delayed such that while the duration of sleep inertia may be truncated, the initial, most severe period of effects are unaffected by caffeine.

When taken after the sleep period, caffeine decreases sleep inertia, with a 30-min delay. The combination of caffeine intake before a 30-min nap (i.e., the "caffeine nap") is considered the most efficient strategy to restore performance and decrease the risk of sleep inertia, in particular during night shifts.[12] Furthermore, while caffeine is indeed a field-deployable and operationally viable countermeasure in many cases, the relatively long-lasting stimulant effects may be unwanted in situations in which it is preferable for the worker to fall back asleep within a few hours of waking.[40]

Also, the efficiency of caffeine is limited by usual caffeine consumption[16] and genetic background.[17] Moreover, caffeine is associated with secondary adverse effects and could not be a generalized strategy.

The impact of a short burst of exercise on sleep inertia is still debated. Exercise may reduce sleep inertia by targeting key physiological processes on waking. Indeed, physical exercise triggers an activation of the sympathetic system and body temperature. Exercise (30 s) on waking improved subjective sleepiness but not cognitive performance.[34]

There is no evidence that a high cognitive stimulation could decrease the amplitude of the kinetics of sleep inertia, in comparison to a low cognitive demand situation. In 23 young healthy men, after 7.5 h of sleep, Kovac et al.[34] observed that anticipating a stressful task before sleep reduces the psychomotor vigilance test and Karolinska sleepiness scale amplitude of sleep inertia. The impact of cognitive stimulation on sleep inertia needs further laboratory and field studies.

While the relationship of body temperature to sleep onset has been extensively investigated, its relationship to sleep offset has received less attention. Some studies have shown, however, that changes in the distal-proximal temperature gradient after waking correlate with subjective sleepiness.[35] This relationship has been demonstrated across different circadian phases in a multi-nap protocol but has yet to be tested with objective performance measures.[36] It has been proposed that cooling the extremities immediately after waking may accelerate recovery from sleep inertia effects. This effect has yet to be tested with an interventional study.

Other strategies such as light or sound have limited possible beneficial effects.[22,51,54] To date, two studies have investigated the use of brief[22,23] and sustained[51] light exposure after waking to reduce sleep inertia. Bright light exposure has been shown to directly improve alertness and cognitive performance during the day, night, and following sleep restriction.[11] Therefore, there is potential for bright light to improve alertness and performance during the sleep inertia period. However, no study observed a significant improvement in objective performance measures. While these results suggest that both brief and sustained light exposure after waking is of limited effectiveness in reducing sleep inertia effects, it is worth noting that the exposures in these studies were during the day (~07:00 and 13:00). The use of light during nocturnal awakenings may, therefore, have a different effect. One study provides the evidence that light exposure during the last 30 min of usual sleep can increase subjective alertness and improve both cognitive and physical performance after waking and could be a countermeasure to sleep inertia.[57] In another study, it was found that exposure to polychromatic short-wavelength-enriched light immediately after waking from SWS at night may help improve vigilant attention, subjective alertness, and mood.[26] These results need to be confirmed.

Noise can promote arousal and has previously been shown to attenuate low vigilance during sleep deprivation.[45,64] Early investigations on the use of sound to reduce sleep inertia effects have been promising. Tassi et al.[54] exposed participants to pink noise after a 1-h nap at 01:00 and observed that pink noise eliminated the sleep inertia effect observed in the no-noise group. This effect was less obvious when tested at 04:00. The sleep stage at waking was not controlled in this study and may have contributed to mixed results at different test times. Hayashi et al.[23] took a different approach, playing music after waking from a short afternoon nap. While playing music has not been shown to have a long-term alerting effect,[46] its short-term effects may be useful in the context of sleep inertia.[39] Indeed, the authors reported that music reduced subjective sleepiness, and that music preferred by the participants led to improved cognitive performance for up to 20 min after waking. Sound may be an operationally viable (i.e., delivered through headphones) and relatively brief and immediate alerting strategy for use in the field.

To be effective, these recommendations must be integrated into 1) an appropriate Fatigue Risk Management System and crew scheduling practices that minimize acute and chronic sleep deprivation; and 2) good sleep management education for pilots. The first step is probably to evaluate the risk of sleep inertia. Based on the literature summarized above, a planned strategy should be taken into account in order to mitigate sleep inertia amplitude and duration. Many of the following criteria are possible before the flight, before the sleep/nap period, and during sleep inertia after awakening (**Table II**). To mitigate sleep inertia, strategies must be used 1) before the flight in order to decrease sleep debt, which is considered the main risk factor of sleep inertia;[24,25] 2) before the sleep period in order to schedule the sleep and anticipate sleep inertia; and 3) after the sleep period in order to improve awakening.

In conclusion, sleep inertia is characterized by impaired performance and reduced alertness immediately after waking. Sleep inertia effects have been observed on a range of tasks from simple reaction time tests to complex cognitive tasks. Sleep inertia interacts with the homeostatic and circadian processes to influence performance immediately after waking. These effects dissipate asymptotically, with the most significant effects occurring within 15–30 min of waking. However, describing the effects of sleep inertia is complex. Many factors should be considered in different protocols, including prior sleep debt, comparison with a control group (at the same time, which is the most robust choice), sleep duration, sleep stage of awaking, and others.

Many protocols have not been replicated and comparison between studies is difficult. Moreover, many studies have been conducted in laboratory designs using subjective questionnaires and cognitive tests. Extrapolation to pilots' performances is hypothetical, and field studies about sleep inertia in pilots are lacking.

Evidence suggests that waking after acute or chronic prior sleep loss, or from deeper stages of sleep, can exacerbate sleep inertia. Taking rest and sleep periods is the only way for a pilot to maintain performance and prevent fatigue.

Table II. How to Mitigate Negative Effects of Sleep Inertia.

BEFORE FLIGHT	BEFORE SLEEP/NAP PERIOD	AFTER SLEEP/NAP PERIOD
Be fit to fly. Treat sleep disorders (sleep apnea, insomnia, rest leg syndrome).	Evaluate the risk of sleep inertia. (Table I)	Take a coffee (60–80 mg caffeine).
Avoid sleep debt. Improve time in bed and sleep time during the nights before the flight.	Schedule the sleep/nap outside of the circadian period of the physiological night.	Practice physical exercise.
Sleep education. Sleep needs, effect of sleep loss, nap strategies, sleep inertia…	Anticipate the wake-up time 15 min before the duty time.	Expose yourself to intense white or blue light.
Limit wakefulness duration. For example, by taking a nap in the afternoon before a night duty.	Use a progressive awakening alarm (light or sound).	Be aware of the operational situation. Briefing with the pilot in command. Improve situation consciousness.
	If high risk of sleep inertia: - Take a coffee. - Practice short nap (<30 min).	

The development of strategies to mitigate sleep inertia may help to promote sleep periods for pilots on board. Epidemiological studies and evaluation in real-life ecological situations must be conducted to improve the determination of sleep inertia kinetics and possible consequences for pilots' performances. In this literature review, we observed an important need for ecological research and description of how sleep inertia effects operational situations.

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Authors and Affiliations: Fabien Sauvet, M.D., Ph.D., and Vincent Beauchamps, M.D., M.Sc., Institut de recherche biomédicale des armées, Brétigny sur Orge, and UPR 7330 VIFASOM (Vigilance, Fatigue, et Sommeil) team, Université de Paris, Paris, France; and Philippe Cabon, Ph.D., Université Paris Cité and Univ Gustave Eiffel, LaPEA, F-92100 Boulogne-Billancourt, and Welbees, Paris, France.

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Leveraging Space-Flown Technologies to Deliver Healthcare with Holographic Physical Examinations

Adam Levschuk; Jocelyn Whittal; Ana Luisa Trejos; Adam Sirek

INTRODUCTION: Musculoskeletal injuries are one of the more common injuries in spaceflight. Physical assessment of an injury is essential for diagnosis and treatment. Unfortunately, when musculoskeletal injuries occur in space, the flight surgeon is limited to two-dimensional videoconferencing and, potentially, observations made by the crew medical officer. To address these limitations, we investigated the feasibility of performing physical examinations on a three-dimensional augmented reality projection using a mixed-reality headset, specifically evaluating a standard shoulder examination.

METHODS: A simulated patient interaction was set up between Western University in London, Ontario, Canada, and Huntsville, AL, United States. The exam was performed by a medical student, and a healthy adult man volunteered to enable the physical exam.

RESULTS: All parts of the standard shoulder physical examination according to the Bates Guide to the Physical Exam were performed with holoportation. Adaptation was required for the palpation and some special tests.

DISCUSSION: All parts of the physical exam were able to be completed. The true to anatomical size of the holograms permitted improved inspection of the anatomy compared to traditional videoconferencing. Palpation was completed by instructing the patient to palpate themselves and comment on relevant findings asked by the examiner. Range of motion and special tests for specific pathologies were also able to be completed with some modifications due to the examiner not being present to provide resistance. Future work should aim to improve the graphics, physician communication, and haptic feedback during holoportation.

KEYWORDS: augmented reality, holoportation, physical exam, virtual care, shoulder.

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The remote and extreme nature of space presents unique practical constraints for the provision of healthcare to astronauts. Traditionally, government astronauts have been held to strict health standards to decrease overall risk of medical events during spaceflight. Nevertheless, the hostile environment of space continues to result in medical events which are managed in a virtual fashion by terrestrial flight surgeons. In the near future, increased interest from the private spaceflight sector will see the private space economy market valuation grow to an estimated $1 trillion by 2040.[1] With the anticipated increase in humans accessing space, the concomitant increase of potential comorbidities or medical events in low Earth orbit is anticipated to increase. Due to the perceived value of commercial space, individuals may expect terrestrial-quality healthcare as a common standard in low Earth orbit. Furthermore, government deep-space missions will increase the need for autonomous as well as remote-care capabilities.

The role of the flight surgeon during a space mission is the monitoring and consultant management of medical situations as required. Flight surgeons are traditionally terrestrially based and a model has evolved whereby designated crew medical officers are provided with additional training to assist the flight surgeon to provide care in orbit. While the crew medical officer

From the Institute for Earth and Space Exploration, Western University, London, Ontario, Canada.

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Address correspondence to: Dr. Adam Sirek, Schulich School of Medicine & Dentistry, 1151 Richmond St., London, Ontario N6A 5C1, Canada; asirek2@uwo.ca.

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may be a physician, this is not always the case. One limiting factor for the care provision by flight surgeons in the current paradigm is the lack of a complete clinical encounter, including the physical examination. Flight surgeons are constrained by the same limitations as terrestrial physicians reliant on telemedicine and/or videoconferences for clinical encounters. These technologies provide altered anatomical scale, the inability to touch the patient, and a lack of personal connection and separation, serving to attenuate the quality of physical exams flight surgeons and terrestrial physicians conduct remotely.

A potential solution to some of these limitations is the integration of augmented reality (AR), or virtual-reality (VR) headsets—or together called "mixed-reality" technologies. Mixed-reality technologies can blend modern AR communication technology with healthcare delivery hurdles; however, there has been little research into leveraging holographic encounters to facilitate better remote physical exams. Following the patient interview, the physical exam is the most important tool in a physician's toolbox. Traditional videoconferencing distills the physical exam to inspection of the patient, while the anatomy of the patient being observed is not even on a correct anatomical scale. Mixed-reality holographic clinical encounters could help bridge the gap between virtual and in-person physical exams and help restore the quality of physical exams performed in a virtual setting.

A potential application of these technologies is to assess musculoskeletal (MSK) health virtually. MSK injuries are not uncommon in space and occur at a rate of roughly 0.021 per flight day for every astronaut.[12] Muscle atrophy and deconditioning due to prolonged muscle unloading from low gravity during longer spaceflight contribute to joint injury risk and degradative joint changes.[13] Thus, as spaceflight becomes more commonplace, the unloading effects on muscles and joints will become more prominent, and examining MSK health will be critical.

Since the first generation of mixed-reality commercial headset was released in 2016, there has been a variety of research efforts dedicated to applying AR, VR, and mixed-reality technology to current clinical methods. Researchers have used AR to display alphanumerical data, such as patient history, vitals, and lab results.[2] This is advantageous for sharing data with multiple people who are wearing synchronized headsets and for accessing hands-free data when it is important to maintain sterility. Another clinical use for mixed reality is to stream or overlay live or previously captured images into the field of vision of the clinician. Common image streams include x-ray,[3] endoscopy,[4] ultrasound,[5] and MRI.[6] AR has proven instrumental in fostering collaboration among physicians by enabling remote medical experts to seamlessly connect and share the perspective of their counterparts. This capability is exemplified by its capacity to facilitate remote physicians in joining a collaborative session, granting them access to the viewpoint of their collaborating peers and thereby enhancing real-time, interactive medical consultations.[7] AR has also been used for surgical navigation,[8,9] intravenous injection guidance, and medical trainee education.[10,11]

Considering these benefits, the objective of this work was to investigate the feasibility of using novel holographic communication technology to conduct mixed-reality, holographic, remote physical exams in a terrestrial setting to set a foundation for expanding clinical care options in spaceflight. This technology was originally demonstrated during NASA missions and then in a bidirectional fashion during the Axiom-1 mission to the International Space Station in 2022. The Axiom-1 technical demonstration included a blinded evaluation by an Axiom flight surgeon performing a mock examination of a simulated medical condition on orbit to evaluate the benefits and drawbacks of the technology for clinical encounters. This manuscript describes the subsequent evaluation of bidirectional holographic communication at Western University in London, Ontario, Canada, for the purpose of enhanced virtual care delivery.

METHODS

A bidirectional holographic clinical evaluation was set up between a medical student in London, Ontario, Canada, and a healthy adult man in Huntsville, AL, United States. Informed consent was obtained from the simulated patient and medical examiner. All data was collected noninvasively and was a part of standard engineering testing that would otherwise be done during testing of HoloConnect software (Aexa Aerospace, Houston, TX, United States). No clinical scenario was used and both parties were aware that the examination was being performed on a normal upper extremity.

Both the examiner and the subject used a mixed-reality headset (HoloLens 2, Microsoft, Redmond, WA, United States) and 3D scanning camera (Kinetic, Microsoft) to create and reproduce holograms in their environments. HoloConnect software (Aexa Aerospace) was used to create and display the holograms and enable communication.

The HoloLens 2 is an untethered and self-contained mixed-reality headset. It is a wearable device that combines both virtual and augmented reality to allow users to interact with holographic objects and digital information in the physical world around them. The Kinect cameras on both ends of the bidirectional holoportation were used to capture the motions of the examiner and the simulated patient (**Fig. 1**). These cameras have optimal ranges between 1–3 m from the camera and within a 57° horizontal and 43° vertical field of vision. The Kinect LiDAR motion capture cameras, as well as the LiDAR cameras integrated into the HoloLens, permit real-time three-dimensional (3D) scanning and depth perception which allows both parties to interact with their own environment as well as the other party during the holoportation. The camera system allows both parties to move freely within their acceptable optimal motion capture zone, thereby permitting both ends to continue to interact with their own environment while engaging in holoportation.

The format of the physical examination followed the exam outlined in the Bates Guide to Physical Examination and

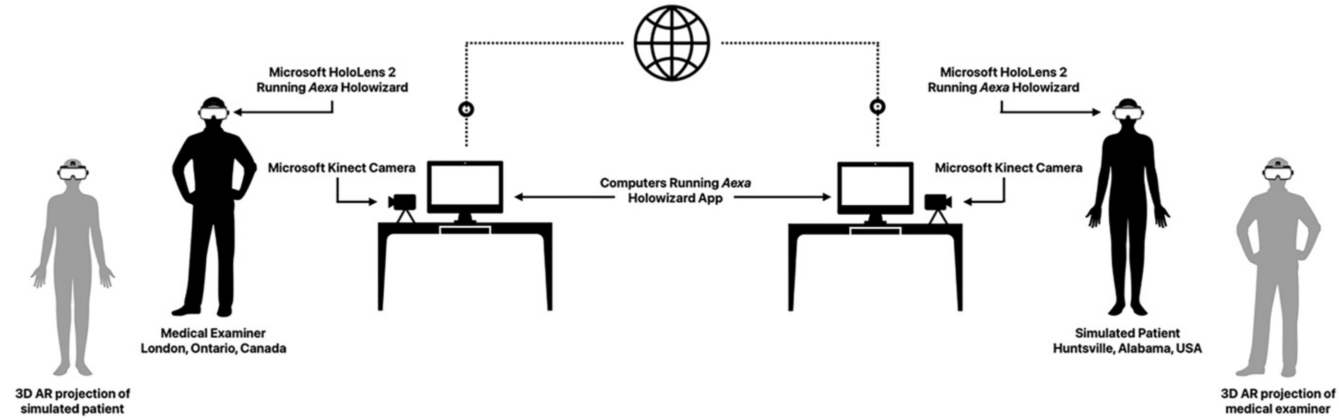

Fig. 1. Materials setup. Both the medical examiner and the simulated patient used a Kinect camera to record their motion. Video streams were connected to Holoconnect software on a local PC. HoloLens 2 headsets running Holoconnect software worn by both people were connected to the same Holoconnect server. Live video from the other's Kinect camera was displayed as a life size 3D augmented reality projection in the other's environment.

History Taking and consisted of inspection of the joint, palpation, and moving of the joint. The exam was slightly modified due to the remote nature of the exam, but still consisted of inspection, palpation, and range of motion testing.

RESULTS

The virtual shoulder exam began with inspection of the shoulder as well as the joints above and below. Similar to traditional videoconferencing, the examiner was able to view all angles and anatomy of the shoulder. However, compared to the small-scale size of patients on computer screens in traditional videoconferencing, the holographic anatomy of the patient was true to anatomical size. The realistic anatomy conferred by the hologram provided the examiner with an increased ability to observe the anatomy; therefore, abnormalities such as swelling, erythema, atrophy, or deformations would have been more obvious if they had been present. Additionally, the realistic anatomy made appreciating muscle tone and bulk closer to an in-person encounter (**Fig. 2**). In a scenario where there is atrophy or an axillary nerve palsy, anatomical changes in the shoulder would have been obvious.

Palpation was performed following inspection. As physical palpation of the hologram was not possible, a clear set of directions for subject self-palpation were developed prior to the exam. In this manner, the examiner could clearly guide the subject through self-palpation. The subject was instructed to palpate with appropriately firm pressure using their second and third fingers. Anatomical landmarks such as the clavicle, coracoid process, acromion process, spine of the scapular, and biceps tendon were used to ensure that the patient was correctly palpating the full anatomy of the shoulder.

For individuals with no medical background, understanding anatomy and relevant nomenclature is not realistic. Thus, alternative physically descriptive names were used to describe anatomical landmarks. Imperfect communication combined with a lack of medical background could lead to errors in self-palpation. Furthermore, it was noted that a person who is experiencing, and is aware of, their own pain may be hesitant to appropriately palpate themselves and report unpleasant findings back to the examiner. Finally, the ability of an individual to palpate their own shoulder is largely dependent on the degree of mobility in their contralateral arm. The spine, medial border, and inferior border of the scapula could be particularly difficult for a mobility compromised person to palpate. Overall, the lack of true palpation was felt to be a shortcoming of this technology despite attempts to guide self-palpation of the subject.

Range of motion in all six degrees of freedom were completed successfully. The true anatomical size of the holograms

Fig. 2. Holographic inspection. Holoportation image allows the forearm muscle definition to be appreciated by the examiner.

Fig. 3. Holographic range of motion. Examiner guiding participant through flexion range of motion testing.

made potential key findings, such as momentary subluxation and scapular dyskinesia, easy to assess (**Fig. 3**).

It was noted during the evaluation that the HoloConnect software was not as high-definition as popular videoconferencing platforms such as Zoom, Microsoft Teams, and WebEx. However, the granularity of the holograms was sufficient such that individual forearm muscles on a person could still be appreciated.

DISCUSSION

A common drawback of virtual health appointments is that telemedicine feels less personal and poses a threat to the gravity of the physician-patient relationship. This deficit may be the reason why virtual environments reduce rapport between physicians and patients and make alliance building more challenging.[14] Holographic encounters can help overcome this problem by creating a tangible sense of presence between physicians and patients due to their ability to place a life-size 3D representation of the individual in anatomical size within the physical space that one is occupying.

This technology demonstrated effective inspection, aided by the life-sized hologram and despite the lower resolution of imagery compared to modern two-dimensional comparable technologies. Range of motion testing was also very effective with this technology. Drawbacks were noted with the subject-directed self-palpation. The lack of ability to feel the tissue and directly examine the individual was a major drawback to the holographic examination.

Special testing of individual shoulder anatomy is commonly done at the end of a physical exam based upon the general findings and to elicit a greater specificity of the presenting shoulder pathology. Nearly all of the special tests for the shoulder require the examiner to be physically present with the patient in order to provide resistance or physically manipulate the limb being examined. The Hawking's test and Neer's test for shoulder impingement syndrome, as well as the acromioclavicular joint scarf test, all require an examiner to manipulate the limb of the patient, and this cannot be performed in a virtual setting. Both Yerguson's and Speed's tests for bicep tendinopathy require the examiner to provide resistance and thus cannot be done in a virtual setting. A modified version of the Speed's test could be done by having a patient hold a resistance creating device, such as an exercise band, in their hand and having them flex their arm while keeping their hand in a supinated position. The subscapularis liftoff, infraspinatus external rotation, and supraspinatus "empty cans" tests all require the examiner to provide resistance to the patient's movement. Modified versions of these tests could be done by having the patient push against an unmovable wall during the subscapularis lift off test and the infraspinatus external rotation test, and having the patient hold a resistance device in their hand during the supraspinatus empty can test. Finally, the glenohumeral instability test normally requires the examiner to provoke the joint into a feeling of instability; however, some researchers have suggested that this test can be done virtually by having the patient place their arm in a "throwing position" to evoke a feeling of instability.[15] However, this may not be recommended during spaceflight because of the possibility of shoulder subluxation or dislocation. Unfortunately, in addition to requiring special technology, completion of these tests would require specialized equipment, further limiting the ability of the technology for virtual care delivery.

In this technology evaluation, the bidirectional 3D AR communication was shown to facilitate virtual physical MSK exams. Compared to traditional videoconferencing, augmented reality communication could confer advantages that improve the quality of physical exams, as well as improve the physician-patient relationship in a virtual setting. Moreover, the directional 3D augmented reality communication demonstrated here could feasibly be used during spaceflight because the technical specifications of the technologies used here are all available in space.

The authors note that improving the quality of graphics would significantly close the gap between in-person and holoportation visits. Additionally, integration of haptic feedback into holoportation would enhance its realism and give physicians the ability to palpate patients remotely.

Many remote areas in the world do not have access to specialty physicians, but holoportation could offer the opportunity for remote areas to access consultation from physicians in a more wholesome manner. Holographic communication remains an exciting and potentially transformative tool poised to redefine virtual medicine by seamlessly transcending distance, enhancing collaboration, and enabling comprehensive, real-time healthcare delivery to astronauts and people on Earth, in the most remote and challenging settings.

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Authors and Affiliations: Adam Levschuk, M.A.Sc., and Adam Sirek, M.D., M.Sc., Schulich School of Medicine & Dentistry; Jocelyn Whittal, Department of Electrical and Computer Engineering, and Ana Luisa Trejos, M.A.Sc., Ph.D., Department of Electrical and Computer Engineering and School of Biomedical Engineering, Faculty of Engineering, Western University, London, Ontario, Canada; and Ana Luisa Trejos and Adam Sirek, Institute for Earth and Space Exploration, Western University, London, Ontario, Canada.

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Air Transportation Impact on a Late Preterm Neonate

Sheng-Ping Li; Po-Chang Hsu; Chuang-Yen Huang; Po-Wei Wu; Hung-Hsiang Fang

BACKGROUND: Neonatal air transportation is a crucial means of moving critically ill or sick neonates to specialized neonatal intensive care units or medical centers for consultation, regardless of distance or geographical limits. Proper preparation and consideration of air transport can help alleviate medical emergencies and ensure safe delivery. However, crewmembers and neonates may face stress during transportation. To date, there are few studies on neonatal air transportation in Taiwan.

CASE REPORT: We present the case of a late preterm neonate born with neonatal respiratory distress syndrome and polycythemia, who was also diagnosed with patent ductus arteriosus and mild pulmonary arterial hypertension on echocardiography. Due to disease progression, the neonate underwent endotracheal intubation and was subsequently transported to a medical center in Taiwan via a rotary-wing aircraft at 3 d of age. During takeoff and landing, a temporary oxygen desaturation event occurred. The physiological changes in these patients have seldom been discussed. This case emphasizes the important considerations of neonatal transport in Taiwan.

DISCUSSION: The air transport process could be influenced by both the patient's medical condition and environmental factors. In preterm infants with cardiopulmonary conditions, thorough assessment is necessary for ensuring safe transportation.

KEYWORDS: neonatal air transportation, respiratory distress syndrome, polycythemia, preterm infants.

Li S-P, Hsu P-C, Huang C-Y, Wu P-W, Fang H-H. *Air transportation impact on a late preterm neonate*. Aerosp Med Hum Perform. 2024; 95(4):219–222.

Premature infants and other neonates are particularly vulnerable to medical and/or surgical issues and may require urgent evaluation or management. However, providing appropriate medical care for critically ill or sick neonates can be challenging, particularly on offshore islands, where access to specialized medical facilities may be limited. Neonatal air transportation offers a means of safely shifting neonates to neonatal intensive care units or specialty consultation centers, regardless of distance or geographical barriers. Whether using rotary-wing or fixed-wing air ambulances, neonatal transport presents unique challenges for aircrews and neonates, including hypoxia, hypobaria, noise, vibration, temperature changes, and reduced humidity.[3,9] Both crewmembers and neonates may face stresses in the air. Adequate preparation and consideration by hospital staff and crewmembers could help mitigate the effects of aeromedical stressors and ensure safe transportation.

Penghu is located approximately 50 km west of the main island of Taiwan. Three district hospitals provide local medical services. The Tri-Service General Hospital, Penghu Branch, is the main hospital for women and children. Owing to geographical barriers, Penghu is in a relatively isolated area. When emergencies occur, medical evacuation can be a big challenge. However, studies focusing on neonatal transportation are relatively rare. This air transportation case report highlights the essential considerations of neonatal transportation in Taiwan.

CASE REPORT

Written informed consent for all subsequent patient information and clinical images was provided by the patient's legal guardians. Signed informed consent was obtained from the patient's parents in accordance with the Institutional Review

From the Division of Pediatrics, Tri-Service General Hospital Penghu Branch, National Defense Medical Center, Penghu, Taiwan; and the Departments of Pediatrics and Obstetrics and Gynecology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan.

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Address correspondence to: Hung-Hsiang Fang, M.D., Department of Pediatrics, Tri-Service General Hospital, National Defense Medical Center, No. 325, Section 2, Cheng-Kung Road, Neihu 114, Taipei, Taiwan, R.O.C.; spty871029@hotmail.com.

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Board of the Tri-Service General Hospital. The ethics committee approved this study (TSGHIRB No.: A202315041).

A late preterm infant was born to a pregnant woman at 36-6/7 wk gestation via cesarean section due to a history of previous cesarean section and preterm labor. The newborn had Apgar scores of 8 and 9 at 1 and 5 min, respectively. Shortly after birth, the patient exhibited dyspnea, subcostal retraction, and cyanosis. A chest radiograph showed a grade II–III reticulogranular pattern (**Fig. 1**). Therefore, the newborn was transferred to a neonatal intensive care unit, where continuous positive airway pressure was administered. In addition, blood test results showed high levels of hemoglobin (Hb; 23.1 g $\cdot$ dL^{-1}) and hematocrit (Hct; 69.2%), indicating polycythemia. During hospitalization, Hb and Hct levels increased to 24.2 g $\cdot$ dL^{-1} and 70.0%, respectively (**Fig. 2**). Echocardiography revealed patent ductus arteriosus and mild pulmonary arterial hypertension. Despite adjustments to the ventilation strategy, the newborn's respiratory distress persisted and gradually worsened. For managing polycythemia, the physician provided adequate hydration and performed a partial exchange transfusion with 20 ml of 0.9% saline. However, by the third day of life, the newborn's respiratory condition deteriorated further, and endotracheal intubation was necessary to maintain adequate oxygenation. Since the newborn's symptoms persisted and continued to worsen, the medical team determined the need for advanced cardiopulmonary assessment. In response, the attending physician contacted the National Aeromedical Approval Center to request air transportation for the baby. To ensure safe and comfortable transfer, the necessary equipment was prepared, including a transport incubator, respiratory support system, T-piece resuscitator, portable oxygen cylinders, vital sign monitors, and syringe pumps. Before takeoff, a qualified emergency medical technician and medical staff conducted a clinical handover using the Identify, Situation, Background, Assessment, and Recommendation protocol. The rotary-wing aircraft flew at an altitude of 1000 ft (304.8 m) during transport, facing wind from the northeast at a speed of approximately 20–30 mph. Noise and vibration appeared to have an impact on the medical

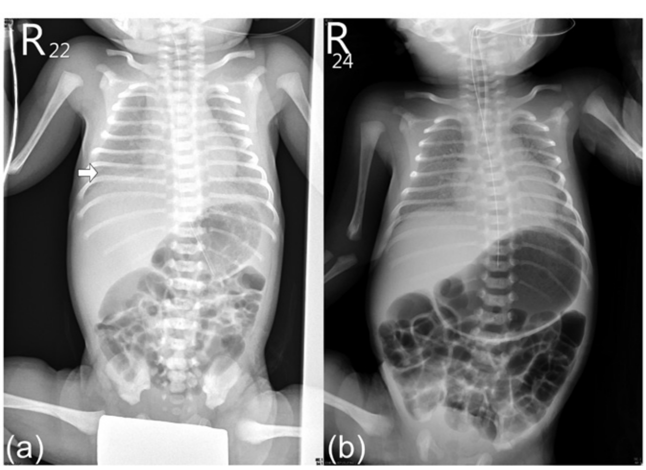

Fig. 1. Chest radiographs: A) shows a reticular granular pattern, grade II–III (arrow); B) taken before air transport.

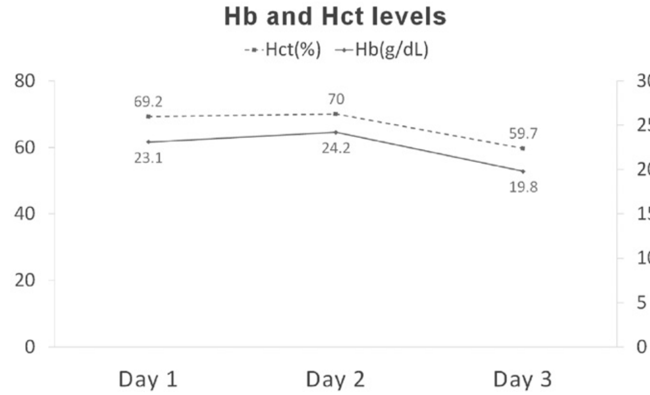

Fig. 2. Hemoglobin (Hb) and hematocrit (Hct) levels were measured at different times both before and following a partial blood exchange.

approach and the patient's condition during the trip. During the patient's journey, the vibrations experienced can potentially lead to physiological responses, such as an increase in heart rate and respiratory rate. These vibrations could induce temporary changes in vital signs, which is an important consideration for the medical team. Prolonged exposure to such vibrations might contribute to patient fatigue, further underscoring the significance of managing this aspect. Moreover, it is worth noting that the presence of pronounced noise and vibration poses challenges not only to patients but also to medical practitioners. These adverse conditions could hinder the ability to conduct precise auscultation, which is a fundamental aspect of accurate medical assessment. Physicians and technicians may find it challenging to discern subtle sounds, impacting the overall quality of their diagnostic procedures. Additionally, the patient's oxygen saturation temporarily decreased to approximately 80% during the takeoff and landing of the rotary-wing aircraft. This flight took 37 min. Upon arrival, an ambulance was ready for subsequent transportation. The patient was transferred to a medical center and received specialized care. After 1-mo follow-up, the patient was discharged from the hospital.

DISCUSSION

Apart from hypoxia, environmental factors, including noise, vibration, temperature, and reduced humidity, could cause stress to both crewmembers and neonates during air transportation.[3,4,9] Therefore, before air transport, it is crucial to consider all these factors.

As altitude increases and atmospheric pressure decreases (hypobaria), gas volume expands. This can affect air spaces within the human body, including the middle ear, sinuses, gastrointestinal tract and lungs, and the pleural, intracranial, and intraocular spaces.[9] As the gas expands, it can cause significant distress to patients during air transportation. Infants may experience respiratory rates ranging between 40 and 60 breaths/min, whereas older children typically have rates of approximately 20 breaths/min.[11] Additionally, the surface area-to-volume ratio is the highest at birth and decreases as a child grows, making pediatric patients more susceptible to thermal energy loss and hypothermia during flight.[11] Therefore, it is important to consider these factors prior to air transportation.

Preterm neonates are at risk of atelectasis due to decreased levels of lung surfactant, resulting in ventilation-perfusion mismatch and hypoxia.[8,11] Aeromedical staff should be aware that in infants the diaphragms are mainly used for respiration because negative intrathoracic pressures are less effective in inspiring air.[8,11] Desaturations were observed in approximately one-third of healthy infants under 6 mo of age during aeromedical transport in a hypobaric hypoxemic condition.[5] Infants tend to become hypoxic due to prematurity or concurrent lung conditions. Moreover, infants easily can experience hypoventilation or apnea when exposed to hypobaric hypoxia during air transport.[8,11] To minimize hypoxia, methods such as oxygen supplementation, maintaining sea-level flight, and reducing disconnection of supplemental oxygen should be employed.[11] Exposure to hypoxic conditions can lead to vasoconstriction of the pulmonary vessels, increasing the risk of right-to-left shunting through a patent foramen ovale and patent ductus arteriosus and nonoxygenated blood returning to the systemic circulation.[11,13] With increasing altitude (hypobaria), expanding intestinal air and pneumothorax are also concerns during flight and mitigating measures such as placing a nasogastric/orogastric tube or chest tube before transport may be necessary. Additional mitigation for hypobaric effects in nonpressurized aircraft includes limiting altitude, as was done in this case. Rapid acceleration and deceleration can lead to a sudden increase in venous cerebral perfusion, which in turn increases the risk of intraventricular bleeding.[1,2,10] Compared with fixed-wing aircraft, typical rotor-wing type cannot provide pressurization, and noise and vibration may be more pronounced.

When planning for neonatal transport, it is important to ensure that essential equipment such as a transport incubator, respiratory support system, T-piece resuscitator, portable oxygen cylinders, vital sign monitors, and syringe pumps are available during transport. However, there may be motion artifacts that would affect the accuracy of the vital sign readings obtained from the monitors during transport. Therefore, it is crucial to prioritize physical assessments rather than solely relying on readings obtained from patient monitors.[4]

The newborn's blood oxygen saturation was unstable during takeoff and landing, which could be attributed to their underlying cardiopulmonary condition. Previous research has indicated that hypoxemia and desaturation are common during air travel in patients with pulmonary hypertension.[10] More than a third of these patients reported symptoms during flights, such as chest pressure/tightness, dizziness, shortness of breath, or palpitations.[7] However, there is limited research on air transportation in neonatal patients, particularly in those with coexisting conditions such as neonatal respiratory distress syndrome or pulmonary hypertension. The hallmarks of clinically significant pulmonary hypertension are hypoxemic right-to-left shunting and cardiac dysfunction, resulting in systemic cyanosis, hypotension, and acidosis.[6] Pulmonary artery pressure increases during simulated air travel in a hypobaric conditions, consistent with previous in-flight observations.[12] Pulmonary hypertension patients face intricate physiological challenges during air transportation due to their compromised cardiopulmonary status. Practitioners should be aware of the potential for exacerbation of right-to-left shunting, alterations in cerebral blood flow, ventilation-perfusion mismatch, hypoxemia, and the risk of cardiac decompensation. The potential impacts on neonates transported by aircraft are illustrated in **Table I**. These conditions can lead to increased stress during flight, particularly during takeoff and landing.

Table I. The Potential Impacts on Neonates Transported by Aircraft.

IMPACT	INFLUENCE
Flight physiology	
Hypobaria	Pressure changes can discomfort neonates and impact their ear and respiratory systems.
Special consideration	
Hypoxia	Reduced blood oxygen saturation
Noise	Short-term exposure to elevated noise levels can lead to fatigue, while long-term exposure to noise can result in hearing loss.
Vibration	Heart rate and respiratory rate are increased, which can contribute to fatigue.
Temperature	Neonates are susceptible to hypothermia in high-altitude environments.
Decreased humidity	Excess fluid loss

This table outlines the key considerations for planning neonatal air transportation.

The success of an air transport mission for a neonate depends not only on factors such as gestational age, bodyweight, or the patient's condition, but also effective collaboration between the hospital staff and aeromedical crew. A well-planned and coordinated approach can minimize the risks and complications that may arise during transport. Beyond the patient's medical condition, environmental factors must also be carefully assessed before planning air transport. Certain cardiopulmonary conditions might affect the transportation process, particularly during takeoff and landing.

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Authors and Affiliations: Sheng-Ping Li, M.D., and Hung-Hsiang Fang, M.D., Division of Pediatrics, Tri-Service General Hospital Penghu Branch, National Defense Medical Center, Penghu, Taiwan; and Po-Chang Hsu, M.D., Po-Wei Wu, M.D., and Hung-Hsiang Fang, Department of Pediatrics, and Chuang-Yen Huang, M.D., Department of Obstetrics and Gynecology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan.

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An Interview with Dr. Stanley White, One of NASA's First Flight Surgeons

Charles R. Doarn

BACKGROUND: In the early days of the National Aeronautics and Space Administration (NASA), medicine in support of the astronauts was led by military experts from the U.S. Air Force as well as experts from the U.S. Navy and U.S. Army. In the early years, a physician with expertise in aerospace medicine was assigned to the Space Task Group and then to NASA. One of these individuals was Dr. Stanley White, a U.S. Air Force physician. To capture more of the early space medicine pioneers, a contract was established between the National Library of Medicine and the principal investigator at the University of Cincinnati to conduct a series of interviews with these early pioneers. An interview with Dr. White took place in his home while he was in hospice care. This audiotaped interview and other written and oral histories within NASA archives and the literature were reviewed to support this work. A series of questions were prepared for the interaction with Dr. White. These questions provided further clarification on his background and contribution. Responses to questions elicited open-ended discussion. The conversation provided a historical summary of Dr. White's contribution to NASA as one of its first flight surgeons.

KEYWORDS: history, flight surgeon, spaceflight, NASA.

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In 1958, the National Aeronautics and Space Administration (NASA) was established from the National Advisory Committee on Aeronautics. During this same period, the Space Task Group (STG) was established by NASA to work at the Langley Research Center in Hampton, VA, in support of the early Mercury Program.[1] The STG eventually became the Manned Spacecraft Center (MSC) (NASA Johnson Space Center) in the early 1960s. There were three military aeromedical consultants, Drs. Stanley C. White [U.S. Air Force (USAF)], William Augerson (U.S. Army), and Robert Voas (U.S. Navy), who were assigned work on life sciences issues related to the human in the system. Dr. White served as the director of the Life Sciences Branch within the Flight Systems Division for Project Mercury.

Dr. White was a graduate of the University of Cincinnati's College of Medicine in 1949. After a short stint in the U.S. Navy, he transferred to the USAF in 1951, where he became a flight surgeon. Over the course of the next several decades, Dr. White's career was intertwined with NASA's Life Sciences and Space Medicine efforts. He held a number of senior leadership positions with NASA's Life Sciences group at the MSC and NASA Headquarters (HQ) in support of Skylab and the Pentagon, and was the president of the Aerospace Medical Association from 1980–1981. **Table I** highlights Dr. White's career path from medical school, aerospace medicine training, and his work with NASA in the Mercury Program, Gemini, Apollo, and Skylab. During his period, he remained in the USAF and was assigned various roles with NASA.[1]

The rich history of NASA's development of space medicine is not as well documented as other equally important tasks at NASA. For example, a lot is written about rockets, satellites, engineering challenges, and politics to name a few. In order to better understand the individuals who impacted space medicine as we understand it today, a contract between the National

From the Space Research Institute for Discovery and Exploration and the Department of Environmental and Public Health Sciences, College of Medicine, University of Cincinnati, Cincinnati, OH, United States.

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Address correspondence to: Charles R. Doarn, MBA, FATA, FAsMA, Director, Space Research Institute for Discovery and Exploration, Office of Research, Professor, Department of Environmental and Public Health Sciences, College of Medicine, University of Cincinnati, ML: 0663, Cincinnati, OH 45221-0663; charles.doarn@uc.edu.

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Table I. Summary Timeline of Dr. White's NASA Career.

YEAR	POSITION	ORGANIZATION
1949	Medical Student Graduate—M.D.	University of Cincinnati
1949	Physician	U.S. Navy
1951	Physician	U.S. Air Force
1952	Training in Aerospace Medicine	Brooks Air Force Base, San Antonio, TX
1953	Graduate student—M.P.H.	Johns Hopkins School of Public Health and Hygiene
1954–1958	USAF Physician, Flight Surgeon	Aeromedical Laboratory, Wright Air Development Center, Dayton, OH Man in Space Soonest
1958	USAF Member of the Aeromedical Team	NASA Space Task Group—Life Sciences Division Langley, VA / Houston, TX
1959–1962	Chief, Life Systems Branch, STG (Medical Operations)	NASA Manned Spacecraft Center
1962–1963	Crew Systems Division Chief	NASA Manned Spacecraft Center
1963	Bioastronautics	Brooks Air Force Base
1966	Manned Orbiting Laboratory / Biomedical Research Program	Brooks Air Force Base
1970–1975	Senior Staff—Medical Payloads for Skylab	NASA HQ, Office of Life Sciences and Office of Manned Spaceflight

Library of Medicine and the University of Cincinnati was awarded to collect oral histories with pioneers in space medicine. Over an 18-mo period (2010–2011), interviews were conducted with a number of space medicine pioneers. The first one with Dr. Arnauld Barer was published in 2017.[2]

Existing oral histories and Dr. White's memoriam, published in this journal, were reviewed. This formed the basis of a series of questions which were sent to Dr. White in preparation for the interview. The interview was conducted by the principal investigator and author of this manuscript with Dr. White on October 6, 2010, in his home in Satellite Beach, FL. He had entered hospice care a few weeks earlier and succumbed to his illness on September 10, 2011.[3]

The conversations began with a background of what the physician, the flight surgeon of the 1950s knew or did not know with regard to space and humans. One of White's statements which stood out was: *"They had broken the sound barrier, but they had not measured anything on the guy. And the best answer that I ever heard was a test pilot say, when asked by one great pontificator in the clinical field, 'how do you know that you were not unconscious while you were doing this maneuver' and the pilot responded, he said 'I had not really thought about that, let me think about it. The fact that I am here, talking to you!'"*

Those early flights on experimental aircraft in the 1950s and Kittinger's high-altitude balloon flights did not have instrumented participants. This predicament resulted in the development of biomedical instrumentation to measure physiological output not only during rest, but also during routine tasks as well. This was before the first flight of Mercury. Before the STG existed, most of this research was conducted through the USAF Bioastronautics Research Program in the late 1950s.

While in the USAF, Dr. White was assigned to Wright-Patterson Air Force Base, specifically Wright Field in Dayton, OH, where he worked on the development of pressure suits, medical monitoring systems, and instrumentation. There were altitude chambers that could be used to conduct simulations and a variety of test facilities. During his time in Dayton, Dr. White indicated that a congressional delegation was visiting the laboratory. Experimental equipment was placed in a storage room so it could not be seen. As you might imagine, a congressman looking for the bathroom stumbled upon the storeroom and equipment and inquired what it was. Dr. White nervously explained and the congressman quipped "*by god it's about time somebody does something like this!*" At that time, that work was not necessarily sanctioned as there was a policy in place—the word "space" was not used by the team at Wright Field or anywhere government funding was provided. Shortly after this, the STG was assigned the responsibility for developing human spaceflight activities and choosing the first astronauts for Project Mercury. Space medicine was an evolutionary step as White recalled: "*You saw a need, you figured out how to do it, which lead to new approaches in medicine even though primitive at the time.*"

Dr. White's next assignment was at Edwards Air Force Base, where the X-15 was to be deployed. In those days, there was no interstate highway system, so Dr. White was driving to California from Ohio with his family and was stopped by the highway patrol near Albuquerque, NM. The officer had a message for him but the phone number was incorrect (it was for the Spanish Embassy). He reported to Edwards and was promptly directed to return back east under orders from his superiors, Generals Bernard Shriver and Don Flickinger. White's new assignment was to work with NASA and the STG under the direction of Robert Gilruth, director of the STG!

White was joined by Robert Voas, a human factors physician from the U.S. Navy, and eventually U.S. Army scientist William Augerson. Their first task was to develop a request for a proposal to build a spacecraft. The original design did not have an accessible window for crewmembers to look out. The engineers at the time did not think an astronaut could observe anything on the surface from space! White and Voas insisted on a window, but it remained an issue. This was finally resolved in part with the help of Dr. Randall Lovelace. He asked Dr. White and Dr. Rufus Hessberg to attend a meeting at Woods Hole, MA. During this meeting, White and others were grilled by the engineers, who said, "*man had no role in controlling, observing, or participating in this movement*." The physicians had to speak "engineer". The real change came when astronauts (the Mercury 7) had a say. The window was part of the design and Gordon Cooper famously watched a train near the Himalayas enter a tunnel, all from the comfort of his spacecraft some 160 mi above the Earth. Postflight, the train schedule was checked, confirming Cooper's observation!

After spending time with NASA, White returned to the USAF and began to work on the Manned Orbiting Laboratory until it was cancelled and then he returned to NASA, initially at Langley and then to the MSC. Early on in human spaceflight, the objective was to get into space, not necessarily development of a robust medical or research effort. The tempo at the time was do and see what comes out. As Dr. White posited, regarding Cooper's flight and the aforementioned train he saw from space, "*Well you can't believe how that opened up just a flood of other questions. And that became feasible. But until you had something like that in hand and proved it to be true.*"

Since much was unknown about the space environment and the astronauts, every step and resultant outcome was primitive and, as White put it, "*every little part you had to fight dog….dog and cat to…because again one thing you have to be sensitive to during this whole period, there were a hell of a lot of people, starting with that Woods Hole meeting I told you we went to, who didn't want man in there in the first place.*" The extramural medical and science community questioned why anyone would fly in a risky mission to space. But against the engineering community and some in the medical community, the first flyers (not called astronauts yet) proved their worth. Each of these individuals were subjected to testing and evaluation as test pilots (self-sufficient, inquisitive, and survivability by controlling the spacecraft). During this time, about 10% of test pilots per year lost their lives, so the Mercury 7 had survived a number of harrowing experiences before their first space mission. Selection of individuals for spaceflight was based on the quest for a 20-yr-old with 30 yr of experience, which was not possible, so the criteria changed. President Eisenhower was the one who finally directed that the individuals come from the cadre of military test pilots. White indicated that the first seven were different as night and day, but worked closely together.

In the early years, the STG was fairly autonomous and would interact with General Charles Roadman, who was detailed to NASA HQ via phone, when medical at MSC needed something. After Mercury, the Gemini and Apollo Programs instituted more structure, albeit small things. Nevertheless, tasks seemed to take longer to complete. As White put it "*Brownian movement*"! The more complex the task or mission, the more individuals had to sign off. This early period brought Dr. Clark Randt from HQ to the MSC to *"organize"* the group.[4] Dr. White commented, "*we had been working our butts off and we were gonna run out of hours as it was, and how we were now gonna be organized and get more hours in.*"

During the Skylab mission, White returned to HQ as a senior medical advisor to support the medical payloads for those missions. He also participated in the first United States/Union of Soviet Socialist Republics three-volume (four books) publication on Space Biology and Medicine.[5,6] This work involved bilateral exchange visits between the two nations.

Dr. White also commented on the next big leap: "*Well I think there are two things. First of all, I would suggest to you that most of the technologies and things supporting space medicine, and this includes instrumentation, data collection, interpretation, and so forth, will continue to progress in the civilian market because it's been captured. Most of the people who are doing this kind of work now hardly will recognize or don't want to recognize that its origin came back from these we've been talking about.*" He also commented on the NASA Syndrome in Melbourne, FL, due to the tremendous stress and strain of those early years of the STG.

Dr. White stressed his commitment to the great endeavor that human space exploration is. His contribution to the National Advisory Committee for Aeronautics, the STG, and NASA helped set the stage for those who have followed in his footsteps. The foundations of monitoring crews, the challenge of the pressures of succeeding in a mostly engineering domain, and the international area serve as the basis of how we practice space medicine today.

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Aerospace Medicine Clinic

This article was prepared by Denis L. Alfin, M.S., M.A., Jelaun K. Newsome, D.O., M.P.H., and Joseph J. Pavelites, M.D., Ph.D.

You are a military flight surgeon assigned to a small aviation medicine clinic. Today you have a number of flight physicals to perform and a handful of return-to-duty determinations. Before you dive into the scheduled work, the front desk of the clinic calls and asks if you can see a pilot who has walked into the clinic with a complaint of "chest pain." Not wanting to ignore a possible emergency, you ask that the patient be immediately escorted into an examination room.

Walking into the examination room, you are quietly relieved to see a young, fit-appearing patient sitting upright, relaxed, and in no apparent distress. The patient is a 29-yr-old male rotary wing student pilot. He is currently in Survival, Evasion, Resistance, and Escape (SERE) training and reports that he has progressive dull/aching pain in his chest. The pain began an indolent course weeks before coming to this training. He explains that the SERE cadre directed him to the clinic as his chest pain is worsening and distracting from his ability to train. He describes the peak pain as an 8/10 and "stabbing" in nature, with difficulty taking in a full breath during exertion. He denies having a cough, fatigue, other symptoms, or contact with other students with similar concerns. He is a never-smoker and his medical record supports his assertions of having no previous history of notable disease, injury, or significant occupational exposures. He denies any chest trauma preceding the symptoms. However, he does report episodes of forceful physical exchanges as part of his training.

Knowing that SERE training can be extremely demanding and not for the faint-of-heart, you are initially skeptical of the veracity of his story. Considering the physical and mental stress that realistic survival training can place on a student, you wonder if he is seeking relief from the course. However, you see that the pulse oximeter displays an oxygen saturation (S_pO_2) of 82% with a heart rate of 105 bpm as the patient sits calmly on the examination table.

The patient is appropriately warm to the touch and does not have an elevated temperature. He is not tender to palpation along the chest wall, there is no discernible anatomic defect, and there is no sign of chest trauma. However, there are signs of mild bruising and minor abrasions on other parts of his body. Auscultation reveals decreased breath sounds on the right with no adventitial sounds detected in any lung fields. The right pulmonary fields are also dull to percussion. His neck veins appear to be distended, but he is a very vascular individual with prominent veins of the upper body.

1. What is the most likely immediate concern to address?
   A. Tension pneumothorax.
   B. Pneumonia.
   C. Asthma.
   D. Costochondritis.

ANSWER/DISCUSSION

1. A. Considering the rough physical treatment that is inherent in the service member's current training, unilateral diminished breath sounds, distended neck veins, and worrisome S_pO_2 levels, you need to address a possible tension pneumothorax.[3] The other choices are less acutely life threatening. Diminished breath sounds and a worrisome S_pO_2 level could be the result of a lower respiratory infection such as pneumonia, considering the training environment he is in.[4] However, the lack of elevated body temperature and other constitutional symptoms makes this less likely. Lack of history of asthma, as well as no irregular lung sounds on auscultation, makes this diagnosis less likely.[5] Physical examination with lack of pain to palpation does not make costochondritis a likely cause of his pain and would not explain his vital signs.[11]

As you think through your treatment plan for this patient, you review your resources: ample supply of sick call medications, a trauma bag with sufficient supplies for combat casualty care, and a base emergency department that is only 5 min away by your clinic's ambulance. Your medic places the patient on

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high flow oxygen. You see that his S_pO_2 is rising quickly and now is above 90% and his heart rate is slowing to 80 bpm.

2. Which of the following is the next best step?
   A. Dispense a metered dose inhaler of albuterol and refer to a pulmonologist.
   B. Send to the emergency department for further acute workup.
   C. Perform a needle decompression.
   D. Dispense a nonsteroidal anti-inflammatory drug for the pain, offer reassurance, and schedule a follow-up for 2 wk.

ANSWER/DISCUSSION

2. B. Considering the improvement in vital signs on high flow oxygen, the lack of patient distress, the ready availability of transport, and the proximity of the emergency department, transfer to a higher level of care is advised over performing the invasive temporizing condition of C in your small clinic. Answer A may be appropriate for a mild asthma exacerbation and D may be fine for costochondritis. However, neither A nor D address the possible immediacy of the situation, not to mention his return to an austere training environment where his condition may worsen.

The patient agrees with your decision to be transported to the emergency room. You direct your staff to begin packaging the patient for transport and you alert the emergency department of the patient's pending arrival. When the patient is well on his way, you inform the patient's training cadre of his status and you mentally review your decisions.

Although your working tension pneumothorax diagnosis was made out of an abundance of caution, you are not completely convinced that it is the cause of his condition. Considering his pleuritic pain, you return to your office and do a deeper dive on his signs and symptoms. You refresh your memory that pulmonary embolism is the most common cause of pleuritic pain as part of a broad differential diagnosis that also includes, but is not limited to, myocardial infarction, pericarditis, aortic dissection, pneumonia, and pneumothorax.[10] As you second guess yourself, you are consoled by the thought that getting him to the emergency room was a good move and you get back to your scheduled patients.

At the end of the workday, you check in with the emergency department. The student aviator's physician allays your fears of a pneumothorax but expresses grave concerns for a possible malignancy. She discusses with you that the chest X-ray reveals a 3 × 4-in (7.62 × 10.16-cm) mass on the lateral view and a 1 × 2-in (2.54 × 5.08-cm) measurement of the mass on the anterior posterior view, located primarily in the mediastinum. The mass is compressing the fields of his right lung.

You immediately start working to get an oncology referral placed and the service member has his first appointment with an oncologist the next day. You also inform the SERE cadre that the service member needs to be removed from the course and that he is temporarily restricted from any flight duties. After the oncologist performs a workup on the patient, you receive a courtesy call outlining the findings. The patient has been diagnosed with a primary mediastinal seminoma.

Somewhat surprised by the diagnosis, you decide to review the literature on seminomas. Seminomas are germ cell tumors (GCTs) that are most commonly found in men between the ages of 15 and 40. The most common presenting symptom of a seminoma is a painless, palpable, testicular mass. Only 20% of GCTs are malignant, with seminomas making up approximately 50% of the malignancies. The mediastinum is the most common location for extragonadal GCTs to reside, although such tumors represent a rare 3–10% of all mediastinal tumors.[12]

3. Which one of the following syndromes sees the development of mediastinal GCTs approximately 10 yr earlier than those without this condition?
   A. Barlow.
   B. Gitelman.
   C. Klein Levine.
   D. Klinefelter.

ANSWER/DISCUSSION

3. D. Klinefelter patients are males born with an extra X chromosome. Hormone abnormalities in this syndrome, i.e., low testosterone with elevated estradiol and luteinizing hormone levels, indicate the presence of a problem with the germ cell line. These germ line irregularities can cause dysregulation of spermatogenesis and predispose the patient to extragonadal malignancies, including earlier onset mediastinal seminomas.[1] Barlow syndrome is a condition that involves the prolapsing of leaflets of the mitral valve. Gitelman syndrome is an autosomal recessive kidney disease that features low potassium, magnesium, and calcium levels. Klein Levine is a rare sleep disorder with excessive daytime somnolence and cognitive/mood changes. These three syndromes are not correlated with the premature development of mediastinal tumors.

The patient underwent surgery for removal of the primary mediastinal seminoma. Following successful removal of the tumor, he completed four rounds of chemotherapy consisting of bleomycin sulfate-etoposide phosphate-cisplatin (also known as BEP therapy). Follow-up with the patient and his oncologist after recovery from surgery and chemotherapy revealed no complications or permanent sequelae.

4. Classically, which one of the following chemotherapy agents was considered a permanent contraindication to diving and possible aviation?
   A. Bleomycin sulfate.
   B. Etoposide phosphate.
   C. Paclitaxel.
   D. Cisplatin.

ANSWER/DISCUSSION

4. A. Historically, bleomycin was considered to be a permanent contraindication to diving and aviation due to the concern for pulmonary toxicity. According to Lauritsen et al., rates of pulmonary toxicity range from 5 to 16%.[8] However, with careful monitoring of pulmonary function during use, this rate can be decreased. Answers B–D are not typically associated with pulmonary toxicity. Common adverse effects of etoposide include bone marrow suppression and dermatological effects (among other concerns). Paclitaxel is more associated with bone marrow suppression and neuropathy, while cisplatin is historically associated with nephrotoxicity.

With regard to the U.S. Army, the primary documents that pertain to returning to flight duties are the Aeromedical Policy Letters and Aeromedical Technical Bulletins. Within these documents, the main subsection that pertains to the case is the malignancy section that states: "In general terms, waiver authorities will often recommend a return to restricted flying status as long as there is a minimal risk of incapacitation as a result of recurrence, treatment is complete, no residual effects from surgery/treatment are present, and the risk of relapse/CNS relapse is minimal (< 1% per year)."[13] The section on testicular tumors specifically discusses the use of bleomycin: "If the aircrew member does develop bleomycin pneumonitis during therapy, then those aircrew are prohibited from ever being exposed to high (over 40% F_IO_2) concentrations of oxygen. This precludes chamber rides or operations in aircraft with oxygen use as a part of the mission, thus possibly necessitating permanent aeromedical suspension depending on the aviation MOS and airframe in question."[14]

According to the U.S. Navy Aeromedical Reference and Waiver Guide's section on testicular tumors and seminomas, "Stage IIB or III treated with [surgery] plus chemotherapy must complete a 2 year [Limited Duty] LIMDU board, during which time no waiver will be considered. After completion of LIMDU, waiver may be considered provided patient is free from recurrence (normal physical exam, tumor markers negative) and pulmonary function tests show no evidence for oxygen toxicity/hypersensitivity."[9]

In the U.S. Air Force, waiver for trained assets may be considered after 6 mo of stable, asymptomatic surveillance following completion of definitive treatment (2 yr for untrained assets). Additionally, "short-duration waivers for individuals with a history [of] bleomycin pneumonitis requiring return to manned aviation are considered on a case-by-case basis after 1 year of post-treatment asymptomatic stability."[7]

The Federal Aviation Administration (FAA) would address return to flight related to this patient's condition with a special issuance. The aeromedical examiner should defer the certification decision to the FAA. The FAA would require that the examiner submit a current status report, including oncologist's status report, list of medications, treatment records, imaging, tumor markers, laboratory results, operative notes, and pathology reports. If the patient is currently on radiation or chemotherapy, the treatment course must be completed.[2]

The medical standards and recommended practices of the International Civil Aviation Organization (ICAO) are found in Annex 1: Personnel Licensing of the ICAO Manual of Civil Aviation Medicine. The guidelines for malignant disease in the ICAO Manual of Civil Aviation Medicine notes that "current curative or adjuvant chemotherapy is incompatible with certification, and recovery from the effects of such treatments will demand a period of unfit assessment after they have finished. If the pilot has recovered from the primary treatment and, as far as can be assessed with available techniques, there is no residual tumor, then the level of certification will depend on the likelihood of recurrent disease."[6] However, ICAO does not make medical fitness decisions in individual cases.

5. Based on the course of his treatment, what is the next best course of action related to his flying career?
   A. Medical separation from service.
   B. Permanent removal from flight duties; retain in service.
   C. Apply for waiver.
   D. Continue temporary duties not including flying until 5 yr cancer free and then reengage for possible waiver.

ANSWER/DISCUSSION

5. C. As this patient did not ever develop bleomycin pneumonitis during therapy, there are no restrictions from altitude chamber or other sporadic oxygen exposure. It was determined that the patient was free from disease and had recovered from surgery and chemotherapy with no aeromedically significant sequelae. He adequately demonstrated his ability to perform his basic military and aviation duties. As such, his branch of service granted him a waiver and returned him to full flight duties. Answers A and B are not correct, as a trained and able individual who has fully recovered and can safely perform his duties does not need to be separated from the military or from flight duties permanently. Answer D is not correct as none of the services require a 5-yr stability period prior to waiver consideration.

After completing his treatments and meeting all the requirements of his branch, the service member was granted a waiver and returned to SERE training. He continued his flight curriculum and graduated with no further concerns. The patient is currently in remission and is periodically screened for reoccurrence as is required by his branch and the oncologist's recommendations. With your ongoing direction and care, he is enjoying a successful career in military aviation.

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APRIL 1999

General aviation crash characteristics (The Johns Hopkins University, Baltimore, MD): "We analyzed the National Transportation Safety Board's Factual Reports for all airplane and helicopter crashes of general aviation flights that occurred in North Carolina and Maryland during 1985 through 1994 … A total of 667 crashes resulted in 276 deaths and 368 injuries during the 10-yr period in the two states. Of the pilots-in-command involved in these crashes, 146 (22%) died. The case fatality rate for pilots was significantly higher in crashes that occurred between 6 p.m. and 5 a.m. (34%), away from airports (36%), with aircraft fire (69%), or in instrument meteorological weather conditions (IMC) (71%) … Significant correlates of pilot fatality were aircraft fire [odds ratio (OR) 13.7, 95% confidence interval (CI) 6.9-27.2], off-airport location (OR 9.9, 95% CI 5.0-19.6), IMC (OR 9.1, 95% CI 4.3-19.6), nighttime (OR 2.2, 95% CI 1.3-3.7), and pilot age ≥50 yr (OR 1.7, 95% CI 1.0-3.0). Pilot gender, flight experience, principal profession, and type of aircraft (airplane vs. helicopter) were not significantly associated with the likelihood of survival."[1]

APRIL 1974

Crew rest calculator (Federal Aviation Administration, Washington, DC): "A device is described for calculating the rest periods necessary for the physical and mental well-being of an air traveler after long-distance flights. The device is basically a pocket-sized calculator consisting of two concentric discs and a pointer. The larger disc is subdivided in an outer and an inner ring. The outer ring is marked in 10° and 5° intervals, which indicate the travel time in hours and half-hours respectively. The center ring is marked in 10° intervals, which indicate the duration of the rest period in hours. The smaller disc, which is transparent in its center to allow for reading the rest-period times, bears the scales of the additional five factors which determine the duration of the rest period. The overlaying transparent pointer, which can be rotated about the center of the device, provides for the reference setting of each factor, for their addition, and for the reading of the final result" (see **Fig. 1**).[2]

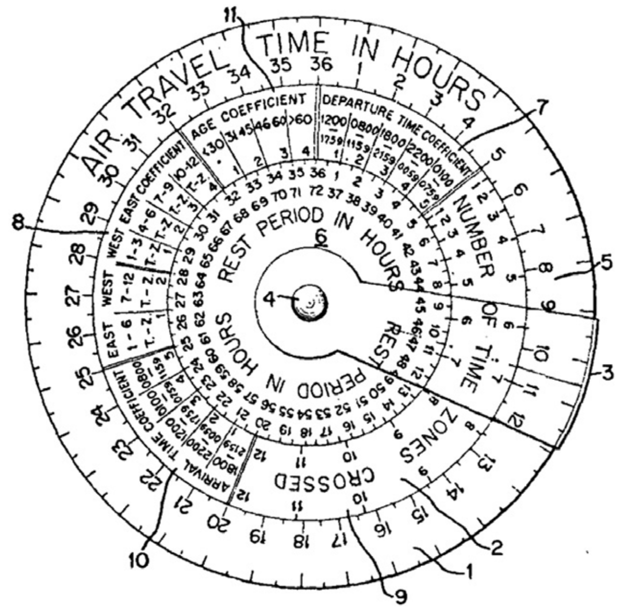

Fig. 1. Physiological rest period calculator.

APRIL 1949

Perceptions of reality (San Jose State College, San Jose, CA, and U.S. Naval School of Aviation Medicine and Research, Pensacola, FL): "Visual cues form the basis for proper orientation during flight, and if they are meager, disorientation may result. This disorientation usually has both visual and nonvisual components. The visual components can be divided into two categories, namely, those which result from deficient stimuli and those which are illusory …

"The observations were made in the rear cockpit of an SNJ-6 aircraft during flight. All visual cues to orientation were eliminated by having the observer close his eyes and cover his head with a heavy, black, sateen cloth. Head movements were minimized by means of a biting board which was held in the mouth throughout each series of trials. In half of the trials the subjects faced straight ahead in the cockpit, and in the remaining half, they twisted the head and body 85 degrees to the left of the line of forward motion of the aircraft …

"These results show that the perception of position in space is a function of the resultant of the force of gravity and the accelerative force acting on the body. The subjects reported clear perceptions of being tilted, which would be interpreted as climbing or diving as far as the behavior of the aircraft is concerned. This is an added source of confusion in orientation resulting from accelerative forces acting on the body during normal flight. These confusions result in disorientation in space and therefore have important implications for flying, particularly when visual cues are lacking and the pilot must rely on the secondary cues presented by the instruments."[3]

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This column is prepared each month by Walter Dalitsch III, M.D., M.P.H. Most of the articles mentioned here were printed over the years in the official journal of the Aerospace Medical Association. These and other articles are available for download from Mira LibrarySmart via https://submissions.miracd.com/asmaarchive/Login.aspx.

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