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Aerospace Medicine and Human Performance

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Aerospace Medicine and Human Performance

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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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AEROSPACE MEDICINE AND HUMAN PERFORMANCE, formerly Aviation, Space, and Environmental Medicine, is published monthly by the Aerospace Medical Association, a non-profit charitable, educational, and scientific organization of physicians, physiologists, psychologists, nurses, human factors and human performance specialists, engineers, and others working to solve the problems of human existence in threatening environments on or beneath the Earth or the sea, in the air, or in outer space. The original scientific articles in this journal provide the latest available information on investigations into such areas as changes in ambient pressure, motion sickness, increased or decreased gravitational forces, thermal stresses, vision, fatigue, circadian rhythms, psychological stress, artificial environments, predictors of success, health maintenance, human factors engineering, clinical care, and others. This journal also publishes notes on scientific news and technical items of interest to the general reader, and provides teaching material and reviews for health care professionals.

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Aerospace Medicine and Human Performance is published monthly by the Aerospace Medical Association. The journal publishes original articles that are subject to formal peer review as well as teaching materials for health care professionals. The editor will not ordinarily review for publication work that is under consideration or has been accepted or published by another journal except as an abstract or a brief preprint. **TYPES OF PAPERS**

The five types of articles specified below should be submitted through the web site and will undergo peer review. Other submissions including Letters to the Editor, Book Reviews, and teaching materials should be submitted by e-mail to the Editorial Office. Letters to the Editor are limited to 500 words of discussion and/or criticism of scientific papers that have appeared in the journal within the past year. If your manuscript does not fit the parameters layed out below, an exception may be granted. Please contact the Editoiral Office to discuss your submission.

Research Articles present the results of experimental or descriptive studies with suitable statistical analysis of results. They should contain an Introduction, Methods, Results and Discussion with a statement of conclusions. Such manuscripts should not exceed 6000 words with approximately 25 references.

Review Articles are scholarly reviews of the literature on important subjects within the scope of the journal. Authors considering preparation of a review should contact the Editor to ascertain the suitability of the topic. Reviews generally may not exceed 6000 words with up to 150 references, but longer reviews of exceptional quality will be considered.

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Short Communications and Technical Notes describe new techniques or devices or interesting findings that are not suitable for statistical analysis. They should contain the same sections as a Research Article but should not exceed 3000 words with approximately 12 references.

Commentaries are brief essays that set forth opinion or perspective on relevant topics. Such manuscripts may not exceed 1000 words with approximately 10 references without tables or figures.

We also accept Historical Notes, and Aerospace Medicine Clinic (formerly You're the Flight Surgeon) articles.

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Each person designated as an author should have made substantial intellectual contributions as specified in the Instructions for Authors. ETHICAL USE OF HUMAN SUBJECTS AND ANIMALS

The Aerospace Medical Association requires that authors adhere to specific standards for protection of human subjects and humane care and use of animals. The methods section of a manuscript must explicitly state how these standards were implemented. Details appear as specified in the Instructions for Authors.

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The language of the journal is standard American English. Authors who are not perfectly fluent in the language should have the manuscript edited by a native speaker of English before submission. Measurements of length, weight, volume and pressure should be reported in metric units and temperatures in degrees Celsius. Abbreviations and acronyms should be used only if they improve the clarity of the document.

PREPARATION OF TABLES AND FIGURES

Tables and figures should be used strictly to advance the argument of the paper and to assess its support. Authors should plan their tables and figures to fit either one journal column (8.5 cm), 1.5 columns (12.5 cm), or the full width of the printed page (18 cm). Tables should be assigned consecutive Roman numerals in the order of their first citation in the text. Tables should not ordinarily occupy more than 20% of the space in a journal article. Figures (graphs, photographs and drawings) should be assigned consecutive Arabic numerals in the order of their first citation in the text. Line drawings of equipment are preferable to photographs. All graphics should be black & white: 1200 dpi for line art; 300 dpi for photos; 600 dpi for combination art. They must be sent electronically, preferably as high resolution TIFF or EPS files. See Documents to Download online for further instructions.

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The Corresponding Author is responsible for providing complete, accurate references so that a reader can locate the original material. References must be formatted in a modified Vancouver style, and listed alphabetically, numbered, then cited by number. An extensive set of examples of different types of references can be found on the web site under Documents to Download. If electronic references are used, they should be readily available to the reader.

MANUSCRIPT SUBMISSION (see details online)

Items for keystroke input:

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When the paper is ready for publication, the printer places on its web site a PDF file depicting the typeset manuscript. The Corresponding Author will be notified by e-mail and is responsible for correcting any errors and for responding to any "Author Queries" (Qs).

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Future AsMA Annual Meetings

May 21 – 25, 2023 Sheraton New Orleans Hotel, New Orleans, LA

May 5 – 9, 2024 Hyatt Regency Chicago, Chicago, IL

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Upcoming FAA Seminars

These are offered by the FAA AME Program office. March 20-24, 2023 Oklahoma City, OK Basic May 23-26, 2023 New Orleans, LA AsMA June 12-16, 2023 Oklahoma City, OK Basic Visit https://www.faa.gov/other_visit/aviation_industry/ designees_delegations/designee_types/ame/seminar_ schedule/ for more information.

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Abstract submission deadline: WEDNESDAY, FEBRUARY 1, 2023, MIDNIGHT ET https://www.uhms.org/meetings/annual-scientific-meeting/ uhms-annual-scientific-meeting-information.html



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- Early Bird Registration runs January 1 31 (Mail registrations must be postmarked with a January date)
- Advance Registration runs February 1 May 12.
- NO CANCELLATIONS OR REFUNDS AFTER MAY 12. A \$50 ADMINISTRATIVE FEE IS APPLIED TO ALL CANCELLATIONS WE <u>STRONGLY</u> ENCOURAGE ONLINE REGISTRATION:

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You <u>MUST</u> be an active member of AsMA in order to register at the member rate. <u>Registration fee does not include membership dues.</u> Fax registration form with credit card information to: (703) 739-9652

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MEMBER	\$450 ⁺	\$550	\$650	
NON-MEMBER	\$725**	\$850*	\$950*	
NON-MEMBER PRESENTER	\$625**	\$750*	\$850*	
	\$325 ⁺	\$400	\$400	
	\$75 ⁺	\$125	\$125	
FAA-AME SEMINAR [§]	\$325†	\$400	\$400	
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* EARLY BIRD REGISTRATION MUST BE PAID IN FULL (INCLUDING ALL EVENTS AND MEAL FUNCTIONS) AT THE TIME OF REGISTRATION.

[§]FEE COVERS ASMA OVERHEAD COSTS. CME CREDIT FOR THE FAA SEMINAR AND ASMA SESSIONS ATTENDED IS INCLUDED.

NOTE: WORKSHOPS ARE LIMITED *** REGISTER EARLY

		FEE	Total Fee
Sun., May 21, 8:00 am – 11:30 am Workshop: "Aerospace Medicine Faculty Development" (MAX 75)			
Sun., May 21, 8:00 am – 4:30 pm Workshop: "Altitude Decompression Sickness – Pathophysiology, Dia Treatment, and Mitigation" (MAX 75)	agnosis,	\$175	
Sun., May 21, 9:00 am – 4:30 pm Workshop: "Establishing Peer Support Programs Across All Aviation (MAX 75)	Sectors	\$150	
EVENTS (NOTE: Advance Purchase Only requires tickets to be purchase during Early Bird & Advance registration – no tickets for these events will be sold onsite)	# OF TICKETS	FEE PER TICKET	TOTAL FEE
Sun., May 21, AsMA Welcome to New Orleans (NOTE: All Attending Event Must Have Tickets)		\$15	
Mon., May 22, 6:00 am, Richard B. "Dick" Trumbo 5K Fun Run/Walk (<i>Advance Purchase Only</i>)		\$15	
Mon., May 22, Aerospace Human Factors Association Luncheon (Advance purchase only)		\$50	
Mon., May 22, Civil Aviation Medical Association Luncheon (Advance Purchase Only)		\$50	
Mon., May 22, Society of US Air Force Flight Surgeons Luncheon (Advance Purchase Only)		\$50	
Mon., May 22, Society of US Army Flight Surgeons Luncheon (Advance Purchase Only)		\$50	
Mon., May 22, US Navy Luncheon (<i>Advance Purchase Only</i>)		\$50	
Mon. May 22, Fellows Dinner (<i>Advance Purchase Only</i>) (MUST BE A FELLOW OR GUEST OF AsMA FELLOW)		\$90	
Tues., May 23, Associate Fellows Breakfast (Advance Purchase Only)		\$50	
Tues., May 23, AsMA Annual Business Meeting (Advance Purchase Only) (Free Attendance; Ticket required for meal)		\$50	
Tues., May 23, Reception to Honor International Members		\$25	
Wed., May 24, Canadian Society of Aerospace Medicine Breakfast		\$50	
Wed., May 24, Aerospace Nursing & Allied Health Professionals Society Luncheon		\$50	
Wed., May 24, Aerospace Physiology Society Luncheon		\$50	
Wed., May 24, Iberoamerican Association of Aerospace Medicine Luncheon		\$50	
Wed. May 24, Society of NASA Flight Surgeons Luncheon		\$50	
Thur., May 25, Space Medicine Association Luncheon		\$50	
Thur., May 25, AsMA Honors Night Banquet (Black Tie Optional)		\$90	
	SUBTOTAL OF	EVENTS	
TOTAL AMOUNT DUE (Registration Fee Subtotal + Workshop + Subtotal of	Events)		

PAYMENT MUST ACCOMPANY FORM. ALL PAYMENTS ARE IN U.S. DOLLARS.

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FAX TO (703) 739-9652. PLEASE REMEMBER TO INCLUDE BOTH SIDES WHEN FAXING. ***USE ONLY <u>ONE</u> METHOD TO REGISTER*** May 21 - 25, 2023 Sheraton New Orleans New Orleans, Louisiana

The WING of AsMA AsMA 93rd Annual Scientific Meeting



REGISTRATION FORM

NOTE: Registration is mandatory for participation in Wing activities.

Please read the entire form before filling out or registering online. Fill out a separate form for each registrant. Advance Registration closes *May 1, 2023*. No refunds *after May 1, 2023*. 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.

Wing Dues (May 2023 – May 2024) \$35.00 /\$40.00 \$				
New Member 2023Renewal2023 Dues Previously Paid Compulsory Registration Fee \$35.00/\$40.00 No\$ Monday, May 22, 2:30 - 4:30 PM The WING Welcome Reception for Registrants only INCLUDED No\$ fuesday, May 23, 8:30 AM - 12:00 PM (Meet in Lobby @ 8:15 AM) wamp Adventure - High Speed Airboat Tour* \$75.00 No\$ SEE IMPORTANT DISCLOSURES <i>OR</i> Fuesday, May 23, 8:30 AM - 12:00 PM (Meet in Lobby @ 8:15 AM) \$55.00 No\$ Wamp Adventure - Swamp Boat Tour <i>OR</i> Fuesday, May 23, 9:30 AM - 2:00 PM (Meet in Lobby @ 9:30 AM) ielf-Guided St. Charles Streetcar Tour Pay as you go No Nednesday, May 24, 10:00 AM - 1:00 PM (Meet in Lobby @ 9:30 AM) Annual Wing Bruncheon & Business Meeting New Orleans School of Cooking \$50.00 No\$ Thursday, May 25, 8:45 AM - 12:30 PM (Meet in Lobby @ 8:45 AM) \$65.00 No\$ Mardi Gras Museum & Mask Making Class TOTAL \$ Name Last Name First Name Spouse's/Sponsor's Name Address City State ZIP Country Phone E-Mail_ Affiliation (please circle one): Army Navy Air Force Corporate Civilian International Exhibitor Register ONLINE at : www.thewingofasma.com <i>OR</i>	Ning Dues (May 2023 – May 2024)	\$35.00 /\$40.00		\$
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The Wing of AsMA Annual Meeting and Tour Information

WELCOME RECEPTION

Monday, May 22, 2:30 – 4:30 PM

Connect with old friends and make some new ones in a relaxed environment at our annual Welcome Reception. <u>Remember to bring a small gift reminiscent of your home city, state or country for the gift exchange and please</u> <u>include a short note letting the recipient know who/where the gift is from</u>. **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 SHERATON NEW ORLEANS HOTEL "Grand Couteau" Room.

TOUR #1 – Swamp Adventure – Airboat Boat Tour* (Gators!!)

Tuesday, May 23, 8:30 AM – 12:00 PM

Meet at 8:15 AM in the Lobby at The Sheraton New Orleans Hotel.

We've chartered an airboat for an exhilarating adventure. You will experience an educational swamp tour and a high-speed airboat ride. Airboats are driven by a 454 Chevy Engine that will produce speeds up to 35 miles an hour. The boats are propelled by a huge fan that will blow air from the back of the boat more than 200 miles an hour. Airboats ride in inches of water and go where traditional boats cannot go! These boats were designed to take you to inaccessible areas of the swamp, which you cannot reach otherwise.

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

*Airboat tours are performed in an open boat. If it rains, you will get wet AND you may get wet without rain, too. In case of inclement weather, the airboat tour may be shortened or replaced with the covered tour boat swamp tour. <u>BECAUSE OF THE NATURE OF THE AIRBOAT RIDE, PREGNANT WOMEN OR PEOPLE WITH NECK OR BACK</u> <u>PROBLEMS CANNOT PARTICIPATE. HEARING PROTECTION IS PROVIDED BY THE COMPANY. YOU CAN PURCHASE</u> <u>INEXPENSIVE RAIN PONCHOS AT THE SWAMP TOUR SNACK SHOP.</u>

<u>TOUR #1A – Swamp Adventure - Swamp Boat Tour (Gators!!)</u>

Tuesday, May 23, 8:30 AM – 12:00 PM

Meet at 8:15 AM in the Lobby at The Sheraton New Orleans Hotel.

You will be very comfortable on this swamp tour boat. Complete with roof, restroom, cushioned seats and windows that can be raised or lowered during cold or rainy weather, along with plenty of standing and walking room. The slow drift of the swamp tour boat through moss draped trees and small waterways will provide ample opportunity for viewing and photography. The tour will be fully narrated. Most captains are natives of the Barataria Swamps with a background in gator hunting, fishing and trapping.

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

TOUR #2 – Self-Guided St. Charles Streetcar Tour

Tuesday, May 23, 9:30 AM - 1:00 PM

Meet at 9:30 AM in the Lobby at The Sheraton New Orleans Hotel.

You and other adventurous Wing members will meet and navigate your way to the St. Charles Streetcar. Don't worry, we'll help get you started, but be sure and register so we know who all will be taking this self-guided independent tour. The St. Charles Streetcar can be boarded a couple of blocks from the hotel. Bring cash. Expect to pay \$1.25 cash to get on the streetcar (but we recommend that you buy a daily pass for \$3.00). The ride takes about 45 minutes each way to ride along St. Charles Street. The route gives you a grand view of some of New Orleans' most beautiful and interesting homes, the Central Business District, Audubon Park, plus Tulane and Loyola Universities. We suggest looking at the stops ahead of time and hopping off to browse in the shops or eat in one of the darling cafes along the way. If you like to explore on your own or with a small group and don't mind handling your own agenda, this tour is for you. Pay as you go for what you want. This tour is one <u>you</u> design as you go.

\$ Pay as you go

\$ 55.00

\$75.00

ANNUAL WING BRUNCHEON & BUSINESS MEETING NEW ORLEANS SCHOOL OF COOKING

Wednesday, May 24, 9:30 AM - 1:00 PM

524 St. Louis Street – New Orleans, LA 70130

Meet in the lobby at 9:30 AM. We can either walk together (0.4 miles or about 12 minutes) or order a ride share to one of The Wing's favorite activities. We'll enjoy a demonstration class where we will "Watch – Learn – Eat". The lesson and meal includes: starter, entrée and dessert. We will learn about New Orleans folklore and how to make tasty dishes that are easy enough to make at home. Our Annual Wing Business meeting will be held in this delightful setting. Of course, there's a lovely shop where you'll find so many fun and unique New Orleans cooking items. This will be a great culinary learning experience with delicious food and a great business meeting. Dietary options are available – Vegan, Gluten Free & Vegetarian. Please email to: **asmawing@gmail.com** if you request one of the dietary alternatives by **MAY 8, 2023.**

Tips are optional but can be given easily and discreetly at your table.

TOUR #3 – Mardi Gras World & Mask Making Class

Thursday, May 25, 8:45 AM – 12:30 PM

Meet in the lobby at 8:45 AM – Transportation is "on our own." We'll share taxis / ride shares and caravan together. It's about **1.5** miles over there. Too far to walk and too close to charter a bus!

Get ready for a Behind the Scenes Tour of Mardi Gras World. The Wing gets to see a special side of Mardi Gras that no one else gets to see! We kick-off with a 15-minute introductory movie. Then, we have an hour walking tour through Mardi Gras World's working warehouse where their artists make over 80 percent of the Mardi Gras props, floats and fun. Be sure to bring your camera and take advantage of the many photo ops.

Next, we'll enjoy a private Mask Making Class. One of Mardi Gras World's certified artists will lead us through designing our very own Mardi Gras mask. They provide all of the magic we need to create our masterpieces, including a premium felt backed mask, glitter, feathers and more. Once our creations are complete, we might agree to wear our works of art as a fun accessory to Honor's Night! We'll head back to the hotel and lunch is on your own.

WING HOSPITALITY ROOM AND REGISTRATION: "Grand Couteau" Room Registration Hours: Sunday, May 21: 1-5 PM Monday, May 22: 10 AM-1:30 PM

Hospitality Room Hours: Sunday: 1-5 PM Monday: 10 AM-1:30 PM

Register Online at: www.thewingofasma.com

or send your completed form and check to: Brenda Clinton, Treasurer 10603 Derby Mesa Ct Colorado Springs, CO 80924 \$65.00

AsMA 93rd Annual Scientific Meeting



"Aerospace and the Next Generation" Sheraton New Orleans Hotel New Orleans, LA, USA May 21 - 25, 2023



REGISTRATION IS OPEN!

Go to https://www.asma.org/scientific-meetings/asmaannual-scientific-meeting/register-for-meeting-andhotel-room and click the link to register for the meeting. Advanced Registration starts February 1 and will continue until May 12, 2023.

PRESIDENT'S PAGE

American Heart Month

Susan Northrup, M.D., M.P.H., FAsMA

Among the many health-related and non-health-related issues claiming February as their month, American Heart Month caught my eye. Cardiovascular conditions remain the number one reason for flying waivers in the United States. Yet as a recent large survey found, aircrew members were likely to delay care longer for cardiac symptoms than the non-flying public because they were concerned about their flying status. This is not uncommon for many conditions. How can we as an aerospace medicine and human factors organization make a difference?

First, we have to acknowledge our population frequently delays care for medical and mental health conditions. There are many reasons—fear of the unknown, potential loss of flying, not believing the symptoms could be real and life threatening, or deciding the symptoms are due to something else. Unfortunately, ignoring symptoms frequently makes things much worse as the disease process progresses. It is much more challenging to return to the flight deck when dealing with significant or endstage disease.

So what can we do about it? In a word: educate. Get the facts and go speak to pilots and other aircrew members. Hang out at your local squadron, aviation group, or flight school. Listen and correct misinformation. Write columns for the local newsletters or magazines. Emphasize early intervention has better outcomes. Talk about prevention. If we can openly discuss a sensitive topic, we get an informed population and that can reduce the stigma of



not being 100% fit. It will also decrease fear. And, maybe, we can save a life.

What else? Stay educated ourselves on the trends in diseases and treatment advances. Follow the research, or participate ourselves. Just the recent progress in cancer treatment is astounding. Progress in medical technology and systems is bringing us closer to the sick bays of futuristic science fiction shows.

We will be critical in affecting a paradigm shift away from pilots and other aircrew members delaying care and it is a challenge worth accepting!

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A Comparison Between Three Computer-Based Cone Specific Color Vision Tests

Julie Lovell; Jeff Rabin

INTRODUCTION: Computerized color contrast sensitivity (CS) tests that aim to determine presence, type, and severity of color vision deficiency have been developed and are available, but data on agreement between tests is lacking. The purpose of the present study was to determine data agreement between three computerized color vision tests.

- **METHODS:** A total of 50 subjects, 25 color vision normal (CVN) and 25 color vision deficient (CVD), were tested with the Konan CCT-HD[®], NCI, and a modified version of the Innova CCT. Sensitivity and specificity were compared across systems as well as differences in log CS values and how these relate to standards used to classify occupational performance.
- **RESULTS:** Each test showed 100% sensitivity for detection of hereditary red-green CVDs as well as type (protan vs. deutan). Each test showed 100% specificity for confirming normal red-green color vision in CVNs. Innova CCT and NCI showed 100% specificity in CVNs and CVDs for S cone CS. Konan CCT-HD[®] showed 96% specificity in CVNs and 92% in CVDs for S cone CS.
- **DISCUSSION:** These findings indicate that each test reliably identifies hereditary CVD and confirms normal color vision. However, the three tests differ slightly in log CS values used to determine pass/fail scores of red-green color vision using a 100-point scale, and all show that protans consistently score lower than deutans on cone CS. Hence, depending on the criterion used in occupational settings, a single score may not prove equitable for individuals who have a protan deficiency.
- **KEYWORDS:** color vision, Innova cone contrast test, pilot color vision standards, Konan Medical cone contrast test, Nordstrom cone contrast test.

Lovell J, Rabin J. A comparison between three computer-based cone specific color vision tests. Aerosp Med Hum Perform. 2023; 94(2):54–58.

number of computerized color vision tests have been developed over the last 25 yr which seek to identify both type (protan, deutan, or tritan) and severity of color vision deficiency (CVD). These tests are also used to confirm normal color vision (CVN). The Cambridge Color Test uses computer generated Landolt-Cs embedded in luminance noise to determine thresholds based on orientation of the gap and expressed as color ellipses in a specified chromatic space.¹ It has proven highly sensitive and efficacious for hereditary and acquired testing.7,17 The Color Assessment and Diagnosis (CAD) test uses dynamic luminance noise as well. The task is a forced-choice identification of the direction of a moving box of different chromaticity than the background, but isoluminant relative to the mean luminance of the background.⁴ The CAD has been highly successful for hereditary, acquired, and occupational applications using a standard score CAD unit metric based on standard deviations from well-established normal means.⁴ In cone specific contrast sensitivity (CS), letters seen only by red (L), green (M), or blue (S) cones are presented in graded steps of cone contrast using a rapid response-driven staircase.^{12–16} For example, L cone letter contrast is computed as a positive Weber contrast:

$$\left(\frac{L_{\text{stimulation in letter}} - L_{\text{stimulation in grey background}}}{L_{\text{stimulation in grey background}}}\right)^*100$$

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It is crucial to comprehend that the L cone letters yield subthreshold contrasts to M and S cones, and the same applies when M cone CS is determined (the letter contrast for both the L and S cones is subthreshold), and when S cones are tested (the letter contrast for both the L and M cones is subthreshold). Additionally, as in the Cambridge and CAD tests, the display luminances are too high to stimulate rods. The first commercial version of the Rabin Cone Contrast Test was developed by Innova Systems, Inc., in collaboration with the U.S. Air Force (USAF). Since then, several additional versions have been designed using Landolt-C targets and all have been refined since the original test fielded by the USAF. Since cone CS, as described herein, is used in the United States for clinical applications and occupational standards by the Department of Defense (DoD) and Federal Aviation Administration (FAA), we chose to compare the sensitivity and specificity of three similar cone CS tests as well as differences in contrast steps, character sizes, and other factors which may impact test efficacy. Hence, in addition to preliminary CVD identification using pseudoisochromatic plate tests and anomaloscope testing, our purpose was to determine data agreement between the Innova Cone Contrast Test³ (Innova CCT, version 19.7.1.4), Konan CCT High-Definition⁵ (Konan CCT-HD[®], version 1.0.70), and Nordstrom Consulting, Inc., CCT⁹ (NCI, version 14). The stimuli of the three tests are displayed in Fig. 1. Throughout the rest of the paper, they will be referred to as the Innova CCT, Konan CCT-HD[®], and NCI, respectively.

METHODS

Subjects

We recruited 50 subjects (mean age 27 ± 9 SD; 34 men and 16 women) from the local community to participate in the study. Exclusion criteria included history of ocular disease or trauma, neurological disease, or systemic disease not controlled medically. Subjects' color vision status was confirmed by the 24-plate Ishihara PIP⁸ and the HMC-Anomaloscope,⁶ which is the gold standard for diagnosing protan vs. deutan CVD and discriminating between dichromacy and anomalous trichromacy. Subjects were divided into two groups, CVN (N = 25, mean age 24 ± 3 ; 10 men and 15 women) and CVD (N = 25, mean age 30 ± 12 ; 24 men, 1 woman; 7 protanomalous, 18 deuteranomalous). There were no dichromats in the subject pool. Each subject provided written informed consent in accord with our IRB-approved protocol.

Equipment and Procedures

Subjects were first administered the 24-plate Ishihara as an initial screening tool. The test was illuminated by the Daylight Illuminator (illuminant C, Precision Vision, Inc.) with room lights off at a distance of 60 cm. Subjects were identified as CVN if they identified at least 12 of the first 14 testable plates correctly, the same criterion used by the DoD. After subjects were classified as CVN or CVD by the Ishihara, the classification was confirmed by anomaloscope testing. The Konan CCT-HD*,



Fig. 1. Picture of computerized color contrast sensitivity tests: A) Konan CCT-HD®; B) Innova CCT; C) NCI.

NCI, and Innova CCT were performed separately for right and left eyes according to manufacturer's instructions. Testing was conducted monocularly at the specified viewing distance (3 ft; 91.44 cm) in an otherwise dark room with habitual correction and added power as needed for presbyopic subjects. No subjects were allowed to wear tinted spectacle or contact lenses. Cone CS test order and which eye was tested first were randomized across subjects.

The Innova CCT also presents letters (20/330 visible only to L and M cone, 20/440 letters visible only to S cones) at progressively lower cone contrasts using a response driven rapid staircase to determine L, M, and S cone letter recognition thresholds. The letter appears briefly (5 s) in the center of the display and the subject uses a mouse to select the letter seen from an adjacent matching display. The version used in this study was adjusted to slightly lower cone contrasts (0.8–16% for L and M cones and 8–128% for S cones) on a Microsoft Surface Display to enable threshold CCT measures comparable the original CRT-based system.^{11,14}

The Konan CCT-HD^{*} isolates cone types using the same luminance and chromaticity approach to present a 20/330 Landolt C with a gap in one of four orientations and a fouralternative forced choice response-driven PSI algorithm allowing subjects to use a keypad to identify the correct gap orientation (up, down, left, or right).¹⁰ This system uses a finer contrast scale to achieve more exact thresholds. The NCI CCT also uses a Landolt C in a manner similar to the CCT-HD, but does not include as extensive a contrast range. In addition, The NCI has a ceiling effect for the S cone stimulus scores.

Statistical Analysis

While all three tests use a 100-point scale based on logarithmic steps in cone contrast and hence cone CS, we converted all 100-point values to log cone CS based on our measures and values specified by each test manufacturer. Specifically, the 100-point scores were converted to log cone CS based on the cone contrasts of each threshold. For example, a Konan 100-point scale score of 98 for the L cone equates to a log CS of 1.88. For the Innova, a 100-point scale score of 90 for the L cone equates to a log CS of 1.89. **Table I** shows examples of the conversion for each test and L and M cone type. This does not lessen the importance of an intuitive 100-point scale for technicians, clinicians, and scientists alike, but is more exacting and accurate to compare tests based on actual contrast levels.

Two-way nested ANOVA with replication was used to determine if there was a difference in log CS between right and left eyes and assess differences between the three tests. Post hoc

 Table I. Examples of 100-Point Scores Converted Log CS Values for L and M Cones.

100-POINT	CONE	KONAN CCT-HD®	INNOVA CCT	NCI LOG
SCORE	TYPE	LOG CS	LOG CS	CS
75	L	1.67	1.65	1.63
55	L	1.47	1.35	1.30
75	Μ	1.65	1.65	1.63
55	М	1.45	1.35	1.30

paired *t*-tests with Bonferroni correction for multiple comparisons was used to determine cone-specific differences within and between tests. Since no difference was found between right and left eyes across tests [CVNs, F(2,1) = 0.05, P = 0.82; CVDs, F(2,1) = 0.51, P = 0.48], the higher log CS of the two eyes was used for analyses of each cone stimulus for both CVN and CVDs since we considered this to be the subject's best effort for that given cone mechanism. Further analysis was conducted to determine if there were differences between test results of normal and anomalous trichromats.

RESULTS

There was a significant difference in CCT log CS between tests [F(2,2) = 2181.45, P < 0.001]. Fig. 2A shows CVN means (± 2 SE) for L and M cone tests, all of which are well within normal limits using log CS values equivalent to \geq 75, and differences were relatively small. Konan L and M cone CS was higher than the Innova and NCI scores (P < 0.001), while Innova S cone CS was higher than Konan and NCI scores (P < 0.03).

Fig. 2B shows results for protanomalous CVDs on the L cone test and results for deuteranomalous CVDs on the M cone test. All values are at least 5 standard deviations below the normal mean for the abnormal cone for each test (Fig. 2A). This result is below the equivalent 75 cutoff score for the CVDs abnormal cone. As CVNs, CVDs also showed a difference between the three cone CS tests [F = 585 (2,2), P < 0.001]. Konan cone CS for CVD cone types was higher than the Innova and NCI scores (P < 0.001), while their normal cone types were not different (P > 0.23).

Each test showed 100% sensitivity for detection of hereditary red-green CVDs as well as type (protan vs. deutan). Each test showed 100% specificity for confirming normal red-green color vision in CVNs.

With CVNs all tests showed 100% specificity for confirming normal L and M cone CS, but Konan CCT-HD^{*} showed 96% specificity in CVNs and 92% in CVDs for S cone CS. That is, regardless of color vision status, the Konan test mis-identifies some observers as tritan deficient, most likely due to the smaller character size used compared to the original CCT and Innova system, which use larger letter sizes for S cone testing near the peak of S cone and L/M cone contrast sensitivity function.^{11,14} More importantly, protanomalous CVDs showed significantly lower scores on all three L cone tests compared to M cone scores for the deuteranomalous CVDs on all three M cone tests (P < 0.001). If a passing score of <75 is applied equally for protan and deutan CVDs, then this may prove inequitable in occupational and related scenarios.

DISCUSSION

Our findings indicate no significant differences between sensitivity of the three computer-based tests to detect the presence and type of CVD. Using the 100-point scale, all CVDs showed



Fig. 2. A) Mean Log CS (± 2 SE) by cone type. The Konan CCT-HD[®] yields higher log CS for the L and M cones. The NCI yields the lowest threshold for the S cone. B) Comparison of deutan and protan mean log CS (± 2 SE). Across tests, protans scored lower than deutans.

scores <75 in each eye for their anomalous cone type on all three tests, indicating 100% sensitivity. All three tests identified normal red-green color vision in CVN subjects (>75 on L and M cone tests). Based on these criteria, all three tests are suitable for occupational application for detection of hereditary CVD if administered appropriately. For example, inadvertent testing at incorrect distances or selecting a 'distance' setting on the test rather than the 'near' setting would produce larger letters and provide incorrect results.

The Konan CCT-HD[®] system yielded higher values for L and M cone CS, likely due to its finer gradation in contrast steps and lower contrasts achieved than either the modified Innova CCT or NCI.¹⁰ The version we tested has a larger display and higher luminance (100 cd \cdot m⁻²) than both the Innova Surface Pro and NCI displays $(30-50 \text{ cd} \cdot \text{m}^{-2})$. Since the Konan CCT-HD[®] uses a 4-alternative forced choice discrimination task vs. a 10-alternative forced letter recognition task, improved scores could derive from guessing, but the superior algorithm for threshold determination in the Konan-CCT likely circumvents this. It is conceivable that fatigue and effort level may have influenced our results; however, since all three tests were conducted in one session in random order this is most likely not an issue and would have been revealed as significant differences in CVNs and CVDs, which were not detected. In addition, practice or transference effects are possible, but unlikely given the agreement between sensitivity and specificity, lower protan than deutan scores across all three tests, and the dissimilarity in exact testing procedures. From an operational perspective, the age range used in this study is in line with other studies using subjects of suitable military occupational training age.¹⁸ However, caution should be applied for generalizing the results for a clinical setting due to the young mean age of the study participants.²

Overall, each test provides reliable classification of CVN and CVD status with acceptable test repeatability indicated by lack of significant differences between right and left eyes, and excellent sensitivity and specificity with a cutoff which reliably distinguishes between CVDs and CVNs. An important finding of this study is, regardless of test, the lower L cone scores in protan CVDs vs. deutan CVDs. Hence pass/fail criteria which allow for CVDs may be enhanced by using separate cutoffs for protans and deutans.

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Financial Disclosure Statement: The authors have no conflicts of interest to report.

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Cardiorespiratory Responses to Voluntary Hyperventilation During Normobaric Hypoxia

Alexander Haddon; Joel Kanhai; Onalenna Nako; Thomas G. Smith; Peter D. Hodkinson; Ross D. Pollock

BACKGROUND:	Unexplained physiological events (PE), possibly related to hypoxia and hyperventilation, are a concern for some air
	forces. Physiological monitoring could aid research into PEs, with measurement of arterial oxygen saturation (Sp02) often
	suggested despite potential limitations in its use. Given similar physiological responses to hypoxia and hyperventilation,
	the present study characterized the cardiovascular and respiratory responses to each.

- METHODS:
 Ten healthy subjects were exposed to 55 mins of normobaric hypoxia simulating altitudes of 0, 8000, and 12,000 ft (0, 2438, and 3658 m) while breathing normally and voluntarily hyperventilating (doubling minute ventilation).

 Respiratory gas analysis and spirometry measured end-tidal gases ($P_{ET} O_2$ and $P_{ET} CO_2$) and minute ventilation. $S_p O_2$ was assessed using finger pulse oximetry. Mean arterial, systolic, and diastolic blood pressure were measured noninvasively. Cognitive impairment was assessed using the Stroop test.
- **RESULTS:** Voluntary hyperventilation resulted in a doubling of minute ventilation and lowered P_{ET} co₂, while altitude had no effect on these. P_{ET} o₂ and S_p o₂ declined with increasing altitude. However, despite a significant drop in P_{ET} o₂ of 15.2 mmHg from 8000 to 12,000 ft, S_p o₂ was similar when hyperventilating (94.7 ± 2.3% vs. 93.4 ± 4.3%, respectively). The only cardiovascular response was an increase in heart rate while hyperventilating. Altitude had no effect on cognitive impairment, but hyperventilation did.
- **DISCUSSION:** For many cardiovascular and respiratory variables, there is minimal difference in responses to hypoxia and hyperventilation, making these challenging to differentiate. S_pO₂ is not a reliable marker of environmental hypoxia in the presence of hyperventilation and should not be used as such without additional monitoring of minute ventilation and end-tidal gases.
- **KEYWORDS:** physiological episodes, arterial oxygen saturation, aircrew physiological monitoring.

Haddon A, Kanhai J, Nako O, Smith TG, Hodkinson PD, Pollock RD. Cardiorespiratory responses to voluntary hyperventilation during normobaric hypoxia. Aerosp Med Hum Perform. 2023; 94(2):59–65.

In recent years, unexplained physiological events (PE) during fast jet flight have been a concern for some military air forces. The symptoms which occur during flight are often described as 'hypoxic-like' and are often transient in nature. Numerous reports of PEs have been made,⁷ but identifying their cause is challenging due to their complex and multifactorial nature, occurrence in almost all phases of flight with symptoms being self-reported by aircrew, and identification having to be inferred from this and engineering/equipment investigation.⁶ Initially PEs were attributed to hypoxia; however, there are a number of factors such as acceleration atelectasis,^{23,24} spatial disorientation, motion sickness, pressure changes, and decompression sickness⁹ that can play a role. One factor that has been implicated in PEs, and in the United Kingdom suggested to account for two-thirds of hypoxic-like events in the Typhoon aircraft over a 10-yr period,⁵ is hyperventilation.

Hyperventilation, defined as an increase in pulmonary ventilation that is out of proportion to the metabolic production

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of carbon dioxide (CO₂), causes a drop in arterial partial pressure of carbon dioxide (P_Aco₂) that can in turn oppose the increase in ventilation. The associated changes in P_ACO₂ and arterial pH will cause, among other things, heart rate to increase¹¹ and cerebral vasoconstriction.¹² This vasoconstriction can lead to reduced cerebral oxygenation and the ensuing cerebral hypoxia can result in symptoms such as personality changes, lack of judgment, short term memory loss, and mental incoordination, all of which can impair performance and are similar to those caused by hypoxia.¹⁵ Hypoxia is defined as inadequate oxygen (O_2) in body tissues with hypoxic hypoxia being the most relevant in aviation.²² The lowering of the arterial partial pressure of oxygen (PAO2) can lead to changes in heart rate and cerebral blood flow.^{1,13,14} Ventilation is also increased through the acute hypoxic ventilatory response,² which is typically evident at altitudes >10,000 ft (>3048 m), although factors such as physical activity may lower this threshold.^{28,29} There are also a number of additional causes of hyperventilation in flight such as whole body vibration, environmental stressors, and elevated temperatures.¹⁵ The most common cause of hyperventilation is likely to be anxiety or stress, with it occurring more regularly in aircrew during training.³ The deterioration in psychomotor performance associated with hyperventilation and hypoxia can be similar, and while aircrew are trained to assume any such symptom is due to hypoxia (and to take corrective action for this), it is important to emphasize that hyperventilation is an alternative potential causative factor.

There are a number of physiological variables and measurement devices that could be used to assess PEs or for routine monitoring of aircrew. One of the most often suggested is the measurement of arterial oxygen saturation (S_nO₂) through pulse oximetry.²⁷ Pulse oximetry is widely used in clinical settings to monitor oxygen saturation and can be used to detect hypoxia; however, there are a number of factors that can influence its readings (e.g., movement, hypotension, vasoconstriction, carboxyhemoglobinemia).¹⁹ Hyperventilation is also known to influence the relationship between the partial pressure of inspired oxygen (P_1O_2) and saturation of oxygen in the arterial blood such that an S_pO₂ reading could be within acceptable limits despite a marked reduction in P_1O_2 and impaired oxygen delivery to the brain,⁸ which could have implications for its use in an aerospace environment.

There are few studies comparing the effects of both hypoxia and hyperventilation on physiological function. Given the growing interest in the use of physiological monitoring in aircrew and its potential role in understanding PEs, it is important to understand the physiological interaction between hypoxia and hyperventilation. This is particularly relevant given the potential limitations of monitoring some physiological variables in an aviation setting. Therefore, the primary aim of the present study is to characterize the cardiovascular and respiratory responses to hypoxic hypoxia of moderate simulated altitudes and to superimposed hypocapnia induced by hyperventilation.

Subjects

This study was approved by the King's College London Research Ethics Committee (HR-19/19-10,435). The study was conducted in accordance with the principles of the Declaration of Helsinki and participants provided written informed consent prior to taking part. A total of 10 healthy subjects (5 men and 5 women) with a mean (SD) age of 24.8 (5.47) yr, height of 1.73 (0.12) m, and mass of 71.5 (8.8) kg completed the study. All participants were nonsmokers with no history of cardiovascular, respiratory, or musculoskeletal disease.

Equipment

All physiological data were recorded and stored using LabChart (v8, ADInstruments, Sydney, Australia) following analog-todigital conversion (Powerlab 16SP, ADInstruments). Throughout testing, heart rate (HR) was continually recorded using 3-lead ECG (LP10, HME, Bolton, UK). Beat-to-beat blood pressure was recorded noninvasively (Finapres 2300, Ohmeda, Englewood, CO, USA) using the volume-clamp method.²¹ The Finapres finger cuff was placed on the third digit of the left hand at the middle phalanx with the hand supported at heart level using a sling. From the recorded blood pressure waveform systolic (SBP), diastolic (DBP), and mean arterial (MAP) blood pressure were determined. S_pO₂ was measured by pulse oximetry (7840, Kontron Instruments, Ismaning, Germany) with the probe placed on the right index finger.

During testing participants wore a low dead-space oro-nasal mask (7450 Series, Hans Rudolph Inc., Shawnee, KS, USA) to which a spirometer was attached (MLT1000L, ADInstruments), allowing respiratory flow rate to be recorded. The recorded flow signal was integrated on a breath-by-breath basis to determine tidal volume (\dot{V}_{T}) while respiratory rate (RR) was determined from the flow signal. Minute ventilation was calculated as the product of V_T and RR and displayed in real time to the participant on a screen directly in front of them. Respired O₂ and CO₂ concentrations were recorded using a rapid response analyzer (ML206-1008, ADInstruments) with the sampling tube connected to a port in the spirometer close to the mouth. Breath-by-breath end tidal partial pressures of oxygen $(P_{ET}O_2)$ and carbon dioxide $(P_{ET}CO_2)$ were determined from the fractional respired O2 and CO2 using peak/trough detection algorithms; barometric pressure was measured on each day of testing and used for the conversion.

To determine the effects of hypoxia and hyperventilation on cognitive function each participant completed the Stroop Test.³¹ The time taken to complete the test and the number of errors were recorded by a member of the experimental team and an overall Stroop score was calculated using the formula:¹⁰

Stroop Score
= Stroop time +
$$\left(\frac{\text{Stroop time}}{100} \times \text{number of errors}\right)$$

Procedure

Each participant attended three sessions, separated by at least 24 h, with the same procedures followed on each day, except at a different simulated altitude. Three simulated altitudes, 0 ft (0 m), 8000 ft (2438 m), and 12,000 ft (3658 m), were investigated using a normobaric hypoxia chamber with the oxygen concentration controlled by a Sporting Edge (Sporting Edge Solutions Ltd., Market Harborough, UK) hypoxia generator. A carbon dioxide scrubber was used to prevent CO₂ build up inside the chamber. On each day of testing participants sat in the hypoxic chamber for 55 min. This began with a 15-min period of breathing normally (NB) followed by cycling at 30 W and 120 W (conducted as part of a larger study and not reported here) for a period of 10 mins. After this there was a period of 15 min rest (while remaining in the hypoxic chamber), which was followed by a 15-min period where the subjects were asked to voluntarily hyperventilate (HV) to a level which doubled their minute ventilation from that recorded during the previous period of NB. To control the level of ventilation participants watched real-time measurements of their minute ventilation on a computer screen placed directly in front of them and were asked to maintain this at the desired level. The Stroop test was administered in the final minute of the NB and HV periods.

Statistical Analysis

For each altitude and breathing condition the average value of each physiological variable was calculated over a 1-min period immediately prior to the Stroop test being administered. \dot{V}_T and \dot{V}_E are reported as BTPS. The normality of the data was confirmed using the Kolmogorov-Smirnov test. A 2-way (voluntary hyperventilation × altitude) repeated measure analysis of variance was conducted. If a significant main effect or interaction was found, post hoc analysis with Bonferroni correction was performed. Significance was determined with an alpha level of 0.05. The number of participants reporting symptoms was recorded but, due to the limited number of symptoms reported, no statistical analysis was performed on these data. Unless otherwise stated data are presented as mean ± SD. All statistical analysis was performed using IBM Statistics v.22 (IBM Corp, Armonk, NY, USA).

RESULTS

By design, there was a main effect of voluntary hyperventilation on \dot{V}_E [*F*(1,9) = 287.87; *P* < 0.001]. The magnitude of increase in \dot{V}_E when hyperventilating at simulated altitudes of 0, 8000, and 12,000 ft (0, 2438, and 3658 m) were ×1.9, ×1.9, and ×2.2, respectively, indicating that subjects were able to achieve the doubling of \dot{V}_{E} , as requested (**Fig. 1**). As would be expected in the presence of hyperventilation, there was a significant reduction in $P_{ET}CO_2$ compared to normal breathing [F(1,9) = 201.76; P < 0.001]. There was no effect of altitude [F(2,18) = 1.69; P = 0.213] or interaction between altitude and hyperventilation [F(2,18) = 1.26; P = 0.777] on $P_{ET}CO_2$ (Fig. 1).

As expected there was a main effect of altitude on $P_{ET}O_2$ [F(2,18) = 549.75; P < 0.001] such that it decreased with an increase in simulated altitude (Fig. 1). The reduction in $P_{ET}O_2$ with altitude was accompanied by a decrease in $S_p o_2 [F(2,18) =$ 37.26; P < 0.001]. A main effect of hyperventilation was found on $S_p O_2$ and $P_{ET} O_2$, with both increasing when voluntarily hyperventilating [*F*(1,9) = 42.31; *P* < 0.001 and *F*(1,9) = 151.71; P < 0.001, respectively; Fig. 1]. For P_{ET}O₂ there was no interaction effect between altitude and hyperventilation [F(2,18) = 1.90;P = 0.860]; however, there was an interaction found with S_pO₂ [F(2,18) = 10.74; P = 0.001]. Post hoc analysis revealed that during both NB and HV, S_pO₂ was significantly lower at 8000 ft than 0 ft (P < 0.001 and $\bar{P} = 0.006$, respectively). During NB $S_p O_2$ was lower at 12,000 ft than 8000 ft (P = 0.011), although this was not the case when hyperventilating. In the presence of voluntary hyperventilation, the $S_p O_2$ of 93.4 ± 4.3% recorded at 12,000 ft was similar to the 94.7 \pm 2.3% recorded at 8000 ft (P = 0.946) despite a 15.2-mmHg reduction in $P_{ET}O_2$. Interestingly the $S_p O_2$ at 12,000 ft while hyperventilating was greater than that recorded when breathing normally at 8000 ft $(90.6 \pm 2.1\%; P = 0.04)$ despite the P_{FT}O₂ being the same $(75.0 \pm$ 6.24 mmHg during HV at 12,000 ft vs. 75.9 ± 4.05 mmHg during NB at 8000 ft; *P* = 0.33).

Respiratory data is shown in **Fig. 2**. The increased \dot{V}_E observed during HV was primarily driven by an increased RR [F(1,9) = 49.70; P < 0.001] with no effect of hyperventilation on \dot{V}_T noted [F(1,9) = 0.097; P = 0.763]. Altitude had no effect on RR [F(1,9) = 0.94; P = 0.409], \dot{V}_T [F(2,18) = 0.20; P = 0.822], or \dot{V}_E [F(2,18) = 1.03; P = 0.376]. Similarly, there was no interaction effect of altitude or hyperventilation on RR [F(1,9) = 0.16; P = 0.851], \dot{V}_T [F(2,18) = 0.69; P = 0.934], or \dot{V}_E [F(2,18) = 1.51; P = 0.247].

A significant main effect of hyperventilation on HR was found [F(1,9) = 18.991; P = 0.002] such that HV resulted in a greater HR than NB. No effect of altitude [F(2,18) = 0.561; P = 0.58] or interaction effect [F(2,18) = 0.361; P = 0.702] was observed on HR (**Table I**). The results relating to MAP, SBP, and DBP are displayed in Table I. There was no effect of altitude, voluntary hyperventilation, or interaction effect on MAP [F(2,18) = 0.98; P = 0.393, F(1,9) = 0.19; P = 0.671, F(2,18) = 1.45; P = 0.264, respectively], SBP [F(2,18) = 1.53; P = 0.243, F(1,9) = 3.36; P = 0.825, F(2,18) = 2.11; P = 0.151, respectively], and DBP [F(2,18) = 0.63; P = 0.542, F(1,9) = 0.70; P = 0.426, F(2,18) = 1.30; P = 0.296, respectively].

Stroop score was significantly worse (greater) with HV (6.8 \pm 1.9 au) compared to NB [4.2 \pm 1.2 au: *F*(1,9) = 42.07; *P* < 0.001]. There was no effect of altitude [*F*(2,18) = 0.406; *P* = 0.672] or interaction of altitude and hyperventilation on Stroop score [*F*(2,18) = 1.20; *P* = 0.324; **Fig. 3**].



Fig. 1. Changes in minute ventilation, partial pressure of end tidal oxygen ($P_{eT}O_2$), carbon dioxide ($P_{eT}CO_2$), and oxygen saturation when breathing normally (dark) and voluntarily hyperventilating (light) while breathing gas mixtures simulating altitudes of 0 ft, 8000 ft, and 12,000 ft (0, 2438, and 3658 m). *Indicates significantly different (P < 0.05) from 20.9% for a given breathing pattern; ^ indicates significantly different (P < 0.05) from 13.2% for a given breathing pattern; # indicates main effect of altitude and ! a main effect of voluntary hyperventilation (P < 0.05). Short bars indicate a significant difference between breathing patterns at a given altitude (P < 0.05).

The number of participants reporting symptoms associated with hypoxia and hyperventilation (hypocapnia) is shown in **Table II**. Overall, very few participants reported any symptoms, with shortness of breath being the most commonly reported, primarily during HV (N = 3). In addition, during HV while at 8000 ft, four participants reported dizziness, but this was not the case when breathing normally or at altitudes of 0 or 12,000 ft.

DISCUSSION

This study presents a number of main findings. Firstly, as expected, both S_pO_2 and $P_{ET}O_2$ declined with increasing simulated altitude. However, when hyperventilating, despite a 15.2-mmHg reduction in $P_{ET}O_2$ with increasing simulated altitude (i.e., a greater degree of environmental hypoxia was present), the S_pO_2 response was blunted such that the recorded values were the same at 8000 and 12,000 ft. The decoupling of the S_pO_2 and $P_{ET}O_2$ response during hyperventilation was further highlighted by a greater S_pO_2 occurring when

hyperventilating at 12,000 ft compared to when breathing normally at 8000 ft despite the $P_{ET}o_2$ being similar. As such, S_po_2 cannot accurately detect environmental hypoxia in the presence of hyperventilation. Secondly, for the simulated altitudes studied, there was no effect of hypoxia on heart rate, although hyperventilation resulted in an elevated heart rate compared to hypoxia. Thirdly, cognitive function, as assessed by the Stroop test, was unaffected by hypoxia but was impaired following hyperventilating. Finally, few symptoms of hypoxia and hyperventilation were noted.

One of the main findings of this study was the discrepancy noted between measures of $P_{ET}O_2$ and S_pO_2 during a hypoxic state when hyperventilating. End tidal oxygen measures have been shown to be an accurate predictor of alveolar gases^{18,20} and are routinely used as a surrogate of arterial gases. In the present study, S_pO_2 and $P_{ET}O_2$ decreased in response to increasing altitude. However, in the presence of hyperventilation there was no difference in the S_pO_2 recorded at 8000 and 12,000 ft simulated altitudes despite a significant decline in $P_{ET}O_2$, indicating a greater degree of hypoxia was present. The significance of this is highlighted in the



Fig. 2. Changes in respiratory rate and tidal volume when breathing normally (dark) and voluntarily hyperventilating (light) while breathing gas mixtures simulating altitudes of 0 ft, 8000 ft, and 12,000 ft (0, 2438, and 3658 m).The ! indicates a main effect of breathing pattern (P < 0.05).

study by the S_po_2 recorded at 12,000 ft while hyperventilating (93.4 ± 4.3%) being greater than the S_po_2 recorded at the lower altitude of 8000 ft (90.6 ± 2.1%) despite similar $P_{ET}o_2$, i.e., hyperventilation raised the S_po_2 above that seen at a lower altitude. This has serious implications for the use of S_po_2 measurements when assessing environmental hypoxia as there is a relative decoupling of the relationship between S_po_2 and P_1o_2 when hyperventilating. This can be explained by the alveolar gas equation with a further contributing factor being a leftward shift in the oxyhemoglobin-dissociation curve associated with the respiratory alkalosis caused by hyperventilation. A consequence of



Fig. 3. Change in Stroop score in response to breathing normally (dark) and voluntarily hyperventilating (light) when breathing gas mixtures simulating altitudes of 0 ft, 8000 ft, and 12,000 ft (0, 2438, and 3658 m).The ! indicates a main effect of breathing pattern (P < 0.05). A higher Stroop score indicates greater cognitive impairment.

the decoupling could be that an individual may be experiencing a significant degree of environmental hypoxia (low P_1O_2) which is not reflected in measures of S_pO_2 .

 $S_p o_2$ is routinely suggested as a key variable for potential aircrew monitoring. The present study shows that without adequate knowledge of the ventilation state of aircrew, this may not be a reliable indicator of environmental hypoxia. Furthermore, $S_p o_2$ measures are routinely used for acceptance testing of oxygen delivery systems. If hyperventilation was present during testing (e.g., due to mask usage or increased breathing resistance associated with the experimental setup), it could result in approval of oxygen delivery systems which are not necessarily providing adequate protection against hypoxia. Currently if $S_p o_2$ is being considered for physiological monitoring or acceptance testing of oxygen delivery systems, it is essential to ensure that as a minimum minute ventilation is recorded and preferably also $P_{ET} o_2$ and $P_{ET} co_2$ to account for the confounding effects that hyperventilation may have.

Hypoxia would be expected to stimulate peripheral chemoreceptors and sympathetic nerve activity (SNA), resulting in an increase in HR. In the present study there was no effect of hypoxia on HR, indicating that the levels studied were below the threshold required to increase SNA.³⁰ Hypocapnia has been suggested to have a modulatory effect on the SNA response to hypoxia.³⁰ This was not the case in the present study, with HV

Table I. Cardiovascular Responses to Hypoxia and Voluntary Hyperventilation.

	0 ft		80	00 ft	12,0	12,000 ft	
	NB	HV	NB	HV	NB	HV	
HR (BPM)#	78.9 (10.1)	86.3 (12.5)	83.4 (11.8)	90.3 (16.3)	81.4 (16.4)	90.2 (18.8)	
SBP (mmHg)	132.2 (8.6)	136.8 (16.5)	125.9 (19.8)	124.3 (17.9)	132.6 (21.9)	128.3 (18.1)	
MAP (mmHg)	101.4 (9.2)	105.4 (11.8)	97.4 (12.5)	95.7 (11.5)	99.9 (12.6)	100.2 (11.0)	
DBP (mmHg)	84.1 (10.2)	88.0 (12.8)	81.4 (13.2)	79.9 (11.5)	81.8 (14.3)	84.5 (12.0)	

NB: normal breathing, HV: voluntary hyperventilation, HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure. #Indicates a main effect of voluntary hyperventilation (*P* = 0.002).

Table II. Number of Participants Reporting Symptoms Associated wi	th
Hypoxia/Hyperventilation (Hypocapnia).	

	0	ft	800	00 ft	12,0	00 ft
	NB	HV	NB	HV	NB	HV
S.O.B.	1	3	0	3	2	3
Fatigue	0	0	0	2	1	1
Dizziness	0	0	0	4	1	1
Light dimming	0	1	0	0	0	0
Trouble concentrating	0	0	1	2	1	2
Blurred vision	0	0	0	0	0	1
Lack of coordination	0	0	0	1	0	0
Tunnel vision	0	0	0	0	0	1
Hot flashes	0	0	0	0	1	0
Cold flashes	0	0	0	0	1	0
Euphoria	0	0	0	0	0	1
Headache	0	0	0	0	0	1
Tingling	0	2	0	2	0	1
Apprehension	1	0	0	0	1	2
Pressure in eyes	0	1	0	0	0	0
Nausea	0	0	0	0	0	1

S.O.B.: shortness of breath. All data are presented as the number (*N*) of participants displaying the symptom.

resulting in a greater HR at all altitudes, but with no interaction effect between altitude and hyperventilation. This likely reflects the lesser degree of hypoxia studied as the modulatory effect of HV may only be present when the severity of hypoxia is sufficient to cause hyperventilatory responses that also affect SNA.¹⁷

The present study simulated altitudes of 8000 and 12,000 ft while also having subjects double their \dot{V}_E to induce hypocapnia. The increases in \dot{V}_E under each hypoxia condition ranged from 1.9-2.2, indicating the subjects were able to achieve the desired level of HV. Similarly, the reduction in $P_{FT}O_2$ shows that the appropriate levels of hypoxia were achieved. Despite this there were no meaningful symptoms of hypoxia or hyperventilation noted other than a small number of participants reporting dizziness during HV. This, combined with similarities in many of the cardiovascular variables when hypoxic and/or hyperventilating, along with the minimal response noted in respiratory variables, highlights the potential challenges associated with physiological monitoring of aircrew. With the growing number of wearable sensors and technological advances in monitoring an individual's physiological response to the environment/exercise, in-flight physiological monitoring has been suggested as a means of monitoring aircrew in real time to identify adverse physiological states associated with the flight environment. However, the flight environment is extremely dynamic, as are the responses of aircrew, with the current findings highlighting the difficulties in distinguishing the physiological response to different stressors; in this case, hypoxia and hyperventilation (and associated hypocapnia). Given similar difficulties have been noted with other potential variables (e.g., transcutaneous Pco_2^{26}) and monitoring devices (wrist mounted $S_p O_2^{16}$) that could be used for physiological monitoring, before in-flight physiological monitoring is considered it is important that further research is conducted to ensure the output of such monitoring can be used to accurately predict the cause of the physiological response so that appropriate corrective action can be taken. This requires careful consideration of which physiological (and environmental) variables are monitored, with validated algorithms applied to identify the cause of the response reliably and accurately.

Cognitive impairment has been a feature noted in many PEs. Hypoxia is known to cause cognitive impairment, the severity of which is largely determined by the degree of hypoxia experienced.²² In the present study there was no effect of hypoxia on cognitive function as assessed by the Stroop test, which is a used as an indicator of selective attention capacity and central processing speed. The lack of hypoxia-related cognitive deficit could potentially be due to the relatively low altitudes investigated (8000 and 12,000 ft equivalents) or the inability of the test used to distinguish the aspects of cognitive function that were affected by the levels of hypoxia studied. In contrast, compared to normal breathing, hyperventilation resulted in significant cognitive impairment. This finding is unsurprising given that hyperventilation and the resultant hypocapnia are associated with elevated blood pH levels, which ultimately cause cerebral vasoconstriction. The consequent alterations in cerebral blood flow and oxygenation can impair cognitive function, which was likely the case in the present study. These findings highlight the importance of considering the role of hyperventilation in the occurrence of PEs with investigation of factors such as increased work of breathing due to the aircrew equipment assembly bulk, inflation of chest counterpressure garments, ejection seat (or torso) harness tightness, or aircrew workload/anxiety required.⁶

Some limitations of the present study should be considered. Firstly, only two altitude equivalents were investigated, 8000 and 12,000 ft. As there is a relationship between altitude and severity of symptoms, it is likely that had higher altitudes been investigated, a greater physiological and possibly cognitive response would have been observed. In addition, the physiological response to normobaric hypoxia may differ from hypobaric hypoxia;^{4,25} therefore, it is possible the present findings may not be equivalent to those that would occur during the hypobaric hypoxia which would occur during flight. Finally, a voluntary hyperventilation model was used where subjects were asked to double their minute ventilation. This is a marked level of hyperventilation; had lower levels of hyperventilation been assessed and consequently less severe hypocapnia developed, the effects of hyperventilation may have been partially ameliorated.

In summary, the present study highlights the similarities and differences in basic physiological responses from exposure to low to moderate levels of hypoxia and hyperventilation/hypocapnia. A main finding of the study is that, in the presence of hyperventilation, measures of S_po_2 alone cannot accurately predict the level of environmental hypoxia experienced. This highlights the potential difficulties in the use of physiological monitoring to provide reliable information to assess the condition of aircrew and whether, and what, corrective action should be taken. In particular, the current data draw into question the use of pulse oximetry for physiological monitoring without the concurrent measurement of end-tidal gases and minute ventilation. Further research is required to identify specifically how an

individual will respond to the different environmental challenges faced by aircrew and how to interpret this data to make informed decisions as to the cause of the physiological response.

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Using Light to Facilitate Circadian Entrainment from Day to Night Flights

Nita Lewis Shattuck; Panagiotis Matsangas; James Reily; Meghan McDonough; Kathleen B. Giles

BACKGROUND: As part of a larger project to provide recommendations regarding limitations and best practices for shifting aviators from day to night operations, a study was conducted to assess the efficacy of high energy visible (HEV) light to shift the circadian rhythm in humans. The study attempted to replicate the patterns of military aviators who could be required to shift abruptly from day to night flight operations.

- **METHODS:** Simulated flight performance and salivary melatonin levels of 10 U.S. military aviators were collected over a 3-night period using a within-subject dim light melatonin onset (DLMO) study design. Data were collected in a laboratory with participants returning home to sleep following each of the three evenings/nights of data collection. Light treatment included a single 4-h exposure of blue-enriched white light (~1000 lux) on night 2. Data collected included melatonin levels, light exposure, sleepiness, cognitive workload, and simulated flight performance.
- **RESULTS:** The average delay in melatonin onset was 1.32 ± 0.37 h (range: 53 min to 1 h 56 min). Sleepiness (P = 0.044) and cognitive workload (P = 0.081) improved the night following the light treatment compared to the baseline. No systematic differences were identified in flight performance.
- **DISCUSSION:** The HEV light treatment successfully delayed the circadian phase of all participants even though participants' ambient light levels (including daylight) outside the laboratory were not controlled. These findings were used to develop circadian synchronization plans for aviators who are asked to transition from day to night operations. These plans will be assessed in a follow-on study in an operational unit.
- **KEYWORDS:** circadian rhythms, circadian misalignment, high energy visible light, night shiftwork, dim light melatonin onset, simulated flight performance.

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Ratigue and sleep issues continue to appear in aviation mishap reports. A recent Naval Safety Center study found 20% of naval aviation accidents over a 5-yr period were caused in part by fatigue and fatigue-related issues, with an estimated cost of \$842M.¹⁶ Compared to day flights, night flights (i.e., flights beginning at the end of evening twilight to sunrise) are more demanding due to multiple factors, including reduced visibility, a heightened reliance on flight instruments, and the possible requirement for night vision goggles. Additionally, the transition from day flights to night flights is especially challenging due to the need to realign one's circadian rhythm, i.e., the ~24-h rhythm of our internal biological clock that regulates the timing of events such as sleep, alertness, mood, and hormone release at specific times of the biological day.

When crewmembers are not accustomed to working nights, night flights may coincide with aircrew circadian low points,

magnifying the already elevated risk levels for night mishaps. This elevated risk is clearly illustrated in a flight mishap that took place in the early morning hours of December 6, 2018, resulting in the deaths of six U.S. Marine Corps aircrew members along with the loss of two aircraft. In the investigation that followed, fatigue was identified as a major contributor to the

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mishap, with the transition from day to night flights specifically called out as a critical source of risk.

Military leaders are frequently confronted with decisions about how best to manage the risks inherent in aviation. The Naval aviation community refers to two documents for managing crew rest and circadian rhythms: Commander Naval Air Forces M-3710.9 and Navy Medicine P-6410.5,8 The information found in these policies has remained essentially unchanged for several years, without specific guidance on safe transitioning between day and night flights. In response to the 2018 mishap report, the Assistant Commandant of the Marine Corps requested the review and revision of these aviation operations policies to update the guidance for the fleet. Consequently, our research team was asked to study the problem and provide recommendations regarding best practices for shifting aviators from day to night operations. An important operational question was the number of days needed to safely adjust when transitioning from day to night flight operations.

The scientific literature clearly shows that circadian rhythms are responsive to environmental cues called "zeitgebers", a German word that means "time-giver". Zeitgebers can entrain and reset one's internal circadian rhythms to align with their external environment.7,24 Physical exercise, the timing and composition of meals, and social interactions are known to affect human circadian rhythms.3,4,25,27,28 However, the dominant and most potent circadian synchronizer is light. When delivered at appropriate times, light can effectively realign the endogenous circadian rhythm. Light can also be an equally powerful circadian disrupter if it is applied inappropriately. Three factors are critical when administering light affecting the circadian system: the timing, the intensity of the light source, and the spectral characteristics of the light. High-energy visible (HEV) light, also known as blue-enriched white light, has spectral characteristics that are most effective at impacting the circadian system.6

Several studies using light have assessed the rate of circadian adaptation when shifting the daily schedule from day to night work. Czeisler and colleagues found that an 8-h exposure to high-intensity light (7000-12,000 lx) at night in a laboratory setting can reset the circadian rhythm by ~1.6 h/d.¹¹ Results from another study, conducted on participants living at home, showed that a 2-h exposure to ~1770-2800 lx of light in the evening was associated with a rate of adaptation of ~ 2 h/d.²⁰ Gander and Samel found an average shifting rate of 2 h/d by using a 5-h exposure to >3500 lx of light at night in their laboratory-based study.²² Dawson and Campbell showed that exposure to bright light in the laboratory (4-h exposure to 6000 lx between 24:00 and 04:00) resulted in an accumulating shift of 5–6 h during the 3-d experiment.¹² In an at-home study, Eastman and Martin¹⁹ demonstrated that a 6-h nighttime exposure to ~5000 lx of light-while also avoiding exposure to light during circadian inappropriate times-resulted in an average phase delay of 2.4 h/d and an average phase advance of 1.6 h/d.^{17,19}

Other studies have assessed the effects of light and melatonin combined with shifting the timing of the sleep schedule. For example, advancing the sleep schedule by 1 h/d, combined with intermittent bright light from light boxes (~5000 lx) for the first 3.5 h after waking in the morning and melatonin taken in the afternoon, can phase advance the circadian clock by ~1 h/d.³³ Paul and colleagues evaluated an afternoon regimen of 3 mg slow-release melatonin with and without next morning 1-h exposure to green light treatment (350 lx) for circadian phase advance.³¹ Results showed the effect of melatonin in the afternoon (average phase advance of 0.72 h when administered independently of light) and exposure to green light upon awakening (average phase advance of 0.31 h when administered independently of melatonin) was additive, demonstrating that multiple circadian zeitgebers may be more effective than a single one.

In conclusion, the findings presented herein suggest that strategic exposure to bright light can be a valuable tool for aviators to use to entrain their circadian rhythm when transitioning from a day to night schedule. However, several limitations were identified in the studies we reviewed. First, some of these studies used body temperature to assess circadian entrainment,^{11,20} not the dim light melatonin onset (DLMO) method that is considered the gold standard for assessing circadian phase.²⁹ Second, applying results of these studies to operational settings in which naval aviators work must be considered carefully. In typical naval aviation units, aviators may be assigned to a regular daily flight schedule, but their work may also involve other assigned duties outside of flying. Consequently, they may be exposed to light at times that are outside the ideal windows for entraining to a night flight schedule. Many of the studies we reviewed were conducted in controlled light conditions.^{20,22} Also, the duration of the light treatment in these studies would not fit into the daily schedule of aviators, whereas exposure to high intensity light has been associated with eye strain and migraine headaches.^{21,36} Given these limitations, our study was specifically designed and conducted to determine the efficacy of HEV light exposure for circadian entrainment in conditions similar to the operational environment that aviators experience.

METHODS

Subjects

A total of 10 individuals volunteered to participate in the study. All participants were qualified aviators from their respective U.S. military communities (Army, Air Force, Marine Corps, and Navy). Participants had varying amounts of flight experience representing diverse platforms. After a preliminary examination of the data, one male participant was excluded from further analysis due to abnormally high salivary melatonin levels throughout both the day and night. Therefore, the analysis was based on nine participants (eight men and one woman, 30 to 44 yr of age, total flight hours = 1282 ± 689). The Naval Postgraduate School Institutional Review Board approved the study protocol and all participants provided written informed consent.

Equipment and Materials

The enrollment questionnaire consisted of a demographic section, items assessing flight experience, use of prescribed or over-the-counter medication, and whether the participant had ever been diagnosed with a sleep-related disorder. In the flight sessions, participants completed the Epworth Sleepiness Scale (ESS) to assess average daytime sleepiness and the Karolinska Sleepiness Scale (KSS) to assess individual situational momentary sleepiness.^{1,23} A modified version of the Bedford Workload Scale (BWS) was used to assess cognitive workload.³⁴

Sleep patterns were assessed by wrist-worn activity monitors (Spectrum Plus; Philips-Respironics; Bend, OR, USA) augmented with self-reported activity logs, validated methods to collect objective sleep data in field studies.² Actigraphic data were collected in 1-min epochs and scored using Actiware software version 6.0.0 (Phillips Respironics). The medium sensitivity threshold (40 counts per epoch) was used, with 10 min of immobility as the criterion for sleep onset and sleep end. All values are the default for this software.

HOBO pendant data loggers were used to assess participants' exposure to ambient light when not in the laboratory. Participants were instructed to wear the device outside their clothing on their upper arm for the duration of the study (approximately 10 d) while awake. Circadian-targeted lighting was administered in the laboratory using light boxes (Circadian Positioning Systems, Inc., Newport, RI, USA). These light boxes were set to a blue boosted bright light setting for the light treatment (~1000 lx) and a dim light setting at all other times (<10 lx). The light boxes were approximately 3–6 ft away from the participant. The position of the light boxes was such that the participants did not look directly at the light. Before each night session, light levels were verified using a CL-500A illuminance spectrophotometer (Konica Minolta, New Jersey, USA). Saliva samples were collected using salivettes (Sarstedt, Nümbrecht, Germany). The samples were centrifuged and chilled immediately and stored at -20°C within 7 h of collection, in accordance with standard practices.¹⁰

Flight performance was assessed using two identical flight simulator systems which included the X-plane 11 flight simulator software by Laminar Research (Columbia, SC, USA) installed on a desktop computer paired with a yoke/pedal/ throttle-lever control interface. The simulated aircraft was a Cessna 152 with analog gauges. Participants performed three ~20-min flight scenarios (A, B, C) of increasing difficulty. Each scenario started in the vicinity of the final approach course 20 mi away from the runway. Participants were instructed to fly the plane using the pretuned instrument landing system to maintain course and descent rate. Flight performance was assessed by three variables: airspeed, horizontal deflection, and vertical deflection. Participants were instructed to fly the plane by maintaining 60 kn as their indicated airspeed. Participants assessed their horizontal and vertical deflection using the course deviation and glideslope indicator. The indicator is designed to give a relative measurement over the width of the localizer beam. The full horizontal deflection of the course deviation and glideslope indicator

Procedure

The 10-d longitudinal within-subject DLMO study was conducted in hybrid conditions. The main experiment was conducted in controlled conditions in the Human Systems Integration Lab, but participants returned home to sleep following each of the three evenings/nights of data collection.

Participants were recruited by a one-time mass email and a study flyer posted on the Naval Postgraduate School student muster page for 2 mo. As shown in **Fig. 1**, the 10-d study was divided into a 7-d sleep/wake control period and a 3-d laboratory data collection period. On the first day of the sleep/wake control period, volunteers completed the enrollment questionnaire and were issued an activity monitor, an activity log, and a light sensor to wear throughout the study. Participants were instructed to maintain their habitual sleep patterns. Actigraphic data were used to determine participants' habitual bedtimes for scheduling their night sessions and to ensure that participants were maintaining a consistent schedule for bedtime and awakening the week prior to the laboratory data collection.

On Day 6, participants conducted a familiarization data collection session that included all three flight scenarios in the simulator. They returned to the lab on the morning of Day 8 for their first laboratory data collection session ("Morning"), completed the preflight questionnaire to assess their state before the commencement of the data collection, and performed the three flight scenarios (A, B, and C, in that order) in simulated daytime settings. The entire lab was illuminated at normal office lighting conditions during this period. After each scenario, the participants provided a saliva sample and completed the KSS and BWS.

Participants returned to the lab 3 h prior to their habitual bedtime in the evening of Day 8 ("Night 1"), Day 9 ("Night 2"), and Day 10 ("Night 3") for their three nighttime data collection sessions. Participants were instructed to have a light meal before their night session and to avoid caffeinated beverages and nicotine for 4 h before arrival. Two separate areas of the Human Systems Integration Lab, a light-controlled area and a flight simulator area, were used for data collection. Upon arriving at the lab, participants stayed in the light-controlled area for the period before the flight tests. Ambient light in the light-controlled area was dim (dim red-enriched light settings of less than 10 lx) on Nights 1 and 3 and bright on Night 2 with lighting provided by the Circadian Positioning Systems light boxes. Specifically, lights during Night 2 were set at a blue-enriched white light setting of approximately 1000 lx (measured at eye level using a spectrophotometer) for the first 4 h following arrival at the lab. After the 4-h exposure to bright light, participants were moved to the flight simulator area and given 30 min in dim light (less than 10 lx) to allow them to dark adapt before performing the three night flights.



Fig. 1. Overview of the experimental protocol. The diagram describes a protocol tailored for a habitual bedtime of 22:00.

Upon arrival for the night sessions, researchers verified that the participants were in good health, had maintained a regular sleep schedule, and had refrained from caffeine or nicotine products for at least 4 h before arriving at the lab. For the first 4 h of each night session, participants were isolated in the light-controlled area, where they were allowed to work on homework, read, watch movies, use the internet, etc. On Nights 1 and 3, all personal electronic devices were kept on the lowest brightness to ensure dim light conditions were maintained.

Each participant completed the KSS and provided a saliva sample every 30 min during each of the three nighttime sessions, for a total of 12 samples per night. The first salivary melatonin sample was collected 2.5 h before their habitual bedtime and the last sample was collected 3 h after habitual bedtime. After each flight, participants completed the KSS and the BWS, and provided a saliva sample. The light levels were measured during each saliva collection using a spectrophotometer. After each data collection session, participants returned home just as they would at the end of a night flight.

The only difference between Night 2 and Nights 1 and 3 was the light treatment, i.e., the bright (~1000 lx) light exposure for the first 4 h when participants were in the light-controlled area. On Night 2, eight salivary samples were collected in bright light conditions while the four final samples (when participants were performing the flight scenarios) were collected in dim light conditions (<10 lx). The timing of the data collections was such that participants were in the bright light setting (~1000 lx) for 3 h before and 1 h after their habitual bedtime. In each data collection session, participants spent approximately 6.5 h in the lab.

Statistical Analysis

Salivary melatonin levels were assessed by the SolidPhase Laboratory, Portland, ME, USA. Melatonin concentration in saliva was determined using radioimmunoassay (Alpco, Salem, NH, USA) with a sensitivity of 0.9 pg \cdot mL⁻¹, intra-assay coefficient of variation of 7.9%, and interassay coefficient of variation of 9.8%. A 4 pg \cdot mL⁻¹ threshold was used to determine the DLMO through linear interpolation.⁹ Circadian phase shifts were calculated by contrasting the DLMO of Night 3 (post-treatment) with Night 1 (baseline). Imputation was applied to seven (1.75%) missing KSS values based on the average of the adjacent values of the participant with the missing data.

Flight performance was assessed by the mean and standard error of three variables, i.e., airspeed deviation from 60 kn, horizontal deflection, and vertical deflection. For each flight, these metrics were aggregated between two points, i.e., at the point at which the participants passed the final approach fix until they were 300 ft above the runway. The Federal Aviation Administration's definition of a final approach is the flight path from the final approach fix, a specific distance from the airport designated on a map, to the runway. Measurements from 300 ft above the runway to landing were excluded because participants had the runway in sight and were using outside visual cues to land.

We conducted a descriptive analysis of participants' demographic characteristics, participant state at the beginning of the main data collection period, and the change in DLMO to assess circadian entrainment. Exposure to ambient light was determined by visual inspection of exposure patterns in the sleep/ wake control and the main data collection periods. Next, we used mixed-effects model analysis to assess differences in KSS and BWS scores between data collections, with a fixed effect of data collection session (Night 1, Night 2, Night 3) and data collection order, and a random effect of subject. Post hoc comparisons were based on Dunnett's test with control accounting for multiple comparisons. Also, mixed-effects analysis was used to assess differences in flight performance between the night data collection sessions. Fixed effects included data collection session (Night 1, Night 2, Night 3), flight profile (A, B, C), and the interactions between data collection session and flight profile, whereas the random effect was the subject. Post hoc comparisons were based on the Tukey honest significant difference (HSD) test, accounting for multiple comparisons.

Statistical analysis was conducted with JMP statistical software (JMP Pro 16; SAS Institute; Cary, NC, USA). Data normality was assessed with the Shapiro-Wilk W test. An alpha level of 0.10 was used to determine statistical significance. The decision to use this alpha level was based on the small number of participants in the study. Summary data are reported as mean \pm SD.

RESULTS

As verified by actigraphy, habitual bedtimes ranged from 21:30 to 00:00. The average ESS score was 4.40 ± 1.78 at the beginning of the day data collection session, with all participants having normal daytime sleepiness (ESS score ≤ 10).

Visual inspection of the light exposure outside the laboratory showed that participants were exposed to ambient light mainly during the morning and early afternoon hours. In general, this pattern was consistent during both the sleep/wake control period of the experiment and the main data collection period. These findings suggest that, when not in the lab, participants were exposed to light at times that are known to counteract the expected phase delay from the light treatment on Night 2. **Fig. 2** shows light exposure for each participant, averaged by hour of day. Participant 9 wore his/her HOBO light logger only during the sleep/wake control period. Average daylight conditions are denoted by the white background.

The DLMO analysis showed that the light treatment on Night 2 successfully delayed the circadian phase of all participants on Night 3. Specifically, the average phase delay was 1.32 \pm 0.37 h, ranging from 53 min to 1 h 56 min.



Fig. 2. Average light exposure by hour of the day and experimental period for each participant. The white backgrounds denote average daylight conditions.

Mixed-effects model analysis showed that sleepiness, as assessed by KSS scores, increased consistently over the course of each of the three nighttime data collection sessions (P < 0.001) and the scores differed between nights (P = 0.006). Post hoc analysis showed that KSS scores in Night 3 (post-treatment) were lower (better) than Night 1 (Dunnet's test with control, P = 0.044) and equivalent to Night 2 (Dunnet's test with control, P = 0.607). These results suggest that reported sleepiness was lower (i.e., participants were more alert) the night following the light treatment compared to the baseline.

Mixed-effects model analysis showed that subjective workload, as assessed by BWS scores, increased consistently over the course of each of the three nights (P < 0.001), and the scores differed among nights (P = 0.001). Post hoc analysis showed that BWS scores on Night 3 (post-treatment) were lower (better) than on Night 1 (Dunnet's test with control, P = 0.081), and equivalent to Night 2 (Dunnet's test with control, P = 0.120). These results suggest that self-reported cognitive workload was lower the night following the light treatment compared to the baseline.

Fig. 3 shows the KSS and BWS scores for all data collection sessions. The morning session was not included in the statistical analysis; however, the corresponding data are included in the diagrams for completeness. The KSS trends are based on a spline smoother with lambda = 1.81. The BWS trends are based on a spline smoother with lambda = 3.24.

Mixed-effects analysis showed that the standard error of airspeed differed between data collection sessions (P = 0.035). Specifically, the airspeed on Night 3 (mean = 1.33 knots, SE = 0.180) was better (less) than on Night 1 (mean = 1.82 knots,





Fig. 3. KSS and BWS scores. Individual participant data (markers) and group trends (lines) are shown.

SE = 0.178; Tukey HSD test, P = 0.027). All other results were not statistically significant (Tukey HSD test, all P > 0.25).

DISCUSSION

We conducted a study to assess the efficacy of bright light exposure for phase-delaying the circadian clock when individuals transition from working days to a night regimen. Our results showed that a single 4-h exposure to the blue-boosted light setting of approximately 1000 lx successfully entrained (i.e., delayed) the circadian phase of all participants an average of 1.32 ± 0.37 h (ranging from 53 min to 1 h 56 min). The importance of this finding becomes clear if we consider that our participants were also exposed to some sunlight throughout the day, partially counteracting the entraining effect of the light exposure in the lab. Theoretically, the magnitude of the phase delay that could be achieved by the light treatment could be increased if aviators adopt and abide by a strict light management protocol throughout the day. Also, the phase delay could be increased further if a battery of carefully aligned synchronization methods could be used, including shifting the daily work/rest schedule and chronobiotics (e.g., melatonin, caffeine).30,32

From a behavioral and light-exposure perspective, the study protocol replicated, to the extent possible, the work/rest patterns of aviators in operational environments when they are working in daylight conditions and are required to shift to night flight operations. Also, the light treatment in the lab (1000 lx) was conservative compared to light levels used in other studies. This decision was based on our intention to increase the external validity of our results by using parameters that could realistically be used in military and other operational settings. Producing extreme bright light intensities requires specialized equipment, which may be challenging to implement in operational settings due to the increased logistical footprint and the associated costs. Also, exposure to high intensity light can lead to adverse health outcomes, e.g., eye strain and migraines.^{21,36} Thus, the results presented here demonstrate that, even when implemented in a manner that is realistic and not ideal (i.e., without strict adherence to light management and without maximizing light intensities), bright light treatment is a valuable tool to aid aviators when transitioning from day to night operations.

Two more issues should be discussed in relation to our findings. First, with the data collected in our study, we cannot quantifiably distinguish the effect of the light treatment per se from the effect of the delayed sleep schedule resulting from the late evening data collection sessions in the laboratory. Results from earlier studies, however, suggest that changes in the sleep-wake cycle provide relatively minimal drive for resetting the human circadian pacemaker.¹⁵ Consequently, we expect that the phase delay identified in our study can be attributed predominantly to the light treatment.

The second issue is that we did not identify any systematic changes in flight performance. This (non) finding may be

explained by our participants' flight proficiency and experience levels and the characteristics of the simulated flights. Our participants were all highly qualified military aviators who were asked to fly a single-engine aircraft for a relatively short period of time in controlled laboratory conditions. Their expertise and flight experience may have masked any potentially deleterious effects of fatigue as well as any positive effects of the light treatment in the simulated flights. Also, the largest effects of fatigue on performance are expected with extended time-on-task,^{14,26} but our aviators were required to perform for a short amount of time (three 20-min flight scenarios). Enrolling only inexperienced aviators, increasing the task difficulty, and/or simulating longer flights may have revealed an effect of the light treatment on performance.

The primary goal of this project was to provide recommendations regarding best practices for shifting aviators from day to night operations by facilitating circadian realignment, thereby mitigating pilot fatigue. Based on the findings of our study, combined with relevant scientific evidence from other authors^{18,30} and existing military regulations,^{5,8,13,35} we developed recommendations that fell into two categories. The first category includes general recommendations for fatigue management, including operational scheduling, sleep hygiene training and education, sleep environment, timing of sleep and naps, light management in the operational environment, use of chronobiotics (e.g., melatonin and caffeine), nutrition, and exercise. The second category of recommendations includes two notional plans for consideration. One plan is designed for aviators transitioning from day to night operations by gradually shifting their schedule, while the second plan is designed for aviators who are unable to gradually transition between schedules due to an abrupt and/or unexpected schedule change.

The study has several caveats. First, we had a small sample of aviators. Second, laboratory conditions cannot replicate the operational environment. To ameliorate this limitation, we used a hybrid study design in which we collected data both in and outside of the laboratory. Participants were allowed to leave the lab at night, return home to sleep, and continue their normal daily activities. This approach increased the external validity of our findings while ensuring adherence to the light intervention in the laboratory. Conducting the study in an operational environment, however, will yield the most valid results. Also, we could not impose any type of crew coordination or radio communication scenarios due to the limitations of the commercial off-the-self simulator we used. Future efforts should revise the flight scenarios to become more challenging and realistic. All the study participants had somewhat consistent sleep schedules before the commencement of the main data collection in the lab. These schedules certainly differ from sleep schedules in operational settings, which may be inconsistent, demanding, and highly stressful. Lastly, we were not able to have a control group due to the limited pool of aviators available to participate in our study, which occurred at the height of the COVID-19 pandemic before vaccines were available. A control group would have allowed us to separate the phase delay effect of the light treatment from the effect of sleeping later due to the experimental protocol.

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Residual Sleepiness Risk in Aircrew Members with Obstructive Sleep Apnea Syndrome

Jonathan Monin; Erik Rebiere; Gaëtan Guiu; Sébastien Bisconte; Eric Perrier; Olivier Manen

BACKGROUND:	Obstructive sleep apnea syndrome (OSAS) is a major problem in aviation medicine because it is responsible for
	sleepiness and high cardiovascular risk, which could jeopardize flight safety. Residual sleepiness after the treatment is not a rare phenomenon and its management is not homogenous in aviation medicine. Thus, we decided to perform a study to describe this management and propose guidelines with the help of the literature.
METHODS:	This is a retrospective study including all aircrew members with a history of OSAS who visited our aeromedical center between 2011 and 2018. Residual sleepiness assessment was particularly studied.
RESULTS:	Our population was composed of 138 aircrew members (mean age 50.1 ± 9.6 yr, 76.8% civilians, 80.4% pilots); 65.4% of

- them had a severe OSAS with a mean Epworth Sleepiness Scale (ESS) at 8.5 ± 4.7 and a mean apnea hypopnea index of 36.2 ± 19.2/h. Of our population, 59.4% performed maintenance of wakefulness tests (MWT) and 10.1% had a residual excessive sleepiness. After the evaluation, 83.1% of our population was fit to fly.
- An evaluation of treatment efficiency is required in aircrew members with OSAS. Furthermore, it is important to have an DISCUSSION: objective proof of the absence of sleepiness. In this case, ESS is not sufficient and further evaluation is necessary. Many tests exist, but MWT are generally performed and the definition of a normal result in aeronautics is important. This evaluation should not be reserved to solo pilots only.
- **KEYWORDS:** obstructive sleep apnea syndrome, sleepiness, maintenance of wakefulness tests, aircrew members.

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t has been known for many years that obstructive sleep apnea syndrome (OSAS) increases the risk of road accidents by a factor of 2 to 3.⁷ We can of course transpose this risk to aeronautics, which requires particular vigilance. The FAA's booklet of recommendations on OSAS8 gives an example of risk in aeronautics. On a daytime flight in the United States in 2008, an airliner with 40 passengers on board flew past its destination airport because both the captain and first officer fell asleep. Once they awakened, the plane was able to reach the destination airport without incident, but with a delay. The investigation uncovered an undiagnosed OSAS in the captain.

OSAS is synonymous of risk to flight safety for three reasons:

- It can be responsible for cognitive and psychological disorders: impaired memory and concentration, longer reaction time, irritability, mood disorders, etc.
- It can generate excessive daytime sleepiness, which can lead to an increased risk of accidents.
- OSAS is considered a cardiovascular risk factor.

This article will focus solely on the risk of sleepiness associated with OSAS. Its aim is to discuss the assessment of sleepiness in aircrew members treated for OSAS.

OSAS can be defined as the repetition of apneas and hypopneas during sleep. Many definitions exist and evolve with different recommendations. We cite the 2014 American Academy of Sleep Medicine definition² presented here.

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Definition 1:

- Polysomnography or home sleep apnea testing demonstrates ≥5 obstructive respiratory events per hour of sleep.
- Presence of one or more of the following:
 - The patient complains of drowsiness, nonrestorative sleep, fatigue, or insomnia symptoms
 - The patient wakes up with breath holding, gasping, or choking.
 - The patient's partner or other observer reports habitual snoring, breathing interruption, or both during the patient's sleep.
 - The patient has been diagnosed with hypertension, mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes mellitus.

Definition 2:

 Polysomnography or home sleep apnea testing demonstrates ≥15 obstructive respiratory events per hour of sleep.

We note the definition is based on both clinical and polysomnographic criteria.

For the French military, it is specified in the 2021 regulation⁴ that sleep apnea syndrome leads to unfitness for pilots, flight mechanics, or air traffic controllers. Aircrew members will then have to ask for a waiver from the military medical commission of aeronautics in order to be able to return to flying duties.

For civilian private and professional pilots, it is specified in the European regulations⁶ that OSAS requires a referral to (or consultation with) the licensing authority. A satisfactory respiratory and cardiological assessment is also required. The acceptable means of compliance¹ specify that a pilot with unsatisfactorily treated sleep apnea syndrome should be assessed as unfit. It is this issue of satisfactory treatment that will be discussed in this article regarding the assessment of sleepiness.

Residual sleepiness in patients with OSAS is generally defined as an Epworth score greater than or equal to 11 despite an appropriate treatment. Its prevalence is estimated at 12% at 1 yr from the start of OSAS treatment.¹²

Multiple causes are described in the literature.^{10,15} The first and foremost cause is a defect in the efficacy, compliance, and tolerance of the treatment (mask or mouthpiece not adapted to, leaks, dryness of the mucous membranes, etc.). It has been shown that the prevalence of residual sleepiness is lower in patients who wear their continuous positive airway pressure (CPAP) for more than 6 hours/night than in those who wear it for less than 4 h (12% vs. 30%).

Once the treatment has been verified, it is also important to question the diagnosis in case of sleepiness in spite of a wellconducted treatment. This involves checking whether the initial problem was indeed OSAS, but also checking there is no other associated sleep pathology, such as restless legs syndrome, narcolepsy, or idiopathic hypersomnia. It is also important to keep in mind that depression is a major cause of sleepiness. It will therefore be important to assess mental health, including the existence of possible mood disorders. Indeed, insomnia or hypersomnia is a criterion in the definition of severe depressive episode in the Diagnostic and Statistical Manual of Mental Disorders V.³ In addition, an epidemiological study in 1989 shown that 40% of patients with insomnia and 46.5% of patients suffering from hypersomnia had an associated psychiatric disorder.⁹

Finally, when all other causes have been investigated, it is commonly described that residual sleepiness can be a sequel to intermittent cerebral hypoxia.^{10,15} In this case, the patient must be referred to a sleep medicine department to discuss medications like wake-promoting agents.

How to assess this sleepiness? It is essential to look for this sleepiness in patients with treated OSAS and even more so in aircrews. In current clinical practice, this screening is essentially based on the Epworth Sleepiness Scale (ESS). In the case of a score compatible with subjective sleepiness, the causes described above are sought. Otherwise, there is generally no further exploration for sleepiness. We can ask ourselves if the ESS alone is sufficient for pilots, but it is also important to keep in mind that the ESS assesses sleepiness in situations of passivity, which does not correspond to piloting activities.

It has been shown in the literature¹⁴ that there is not a good correlation between a subjective test such as the ESS and an objective measure such as the Maintenance of Wakefulness Tests (MWT). The main reason given is that patients with chronic sleep disorders have a poor perception of sleepiness, in which an improvement in the disorder may wrongly suggest that the disorder has disappeared. Moreover, in the context of fitness evaluation, the ESS may not always be honestly reported in a pilot who has been potentially declared unfit since the diagnosis of his/her illness, and who is hoping for a favorable decision from the medical center.

In this context, MWT are an interesting tool. These are sleep laboratory tests that measure a subject's ability to stay awake.¹⁶ They are used in two situations: when hypovigilance is a public or personal safety issue, and to assess response to treatment in sleepy patients. This test is therefore doubly indicated in aircrews.

During this test, the patient is comfortably seated with electroencephalogram (EEG), electrooculogram (EOG), and electromyography (EMG) sensors in a semidark room. He is asked to look ahead, keep his eyes open, and stay awake, fighting sleep as much as possible. It is forbidden to do some waking maneuvers such as looking at the cell phone, reading, chewing gum, pinching oneself, etc. Between tests, the subject must not sleep but may go about his or her business.

This test is repeated four times in the same day, every 2 h, after a good quality sleep the night before the tests. If the subject does not sleep, the test lasts 40 min. Otherwise, the test is stopped as soon as the subject falls asleep (with the need for three consecutive 30-s epochs in the case of stage 1 sleep). The sleep latency corresponding to the average of the four tests is

thus calculated. So, if the subject did not sleep during the test, the average sleep latency is 40 min.

To determine the values that may correspond to a decreased alertness, the MWT results were compared to actual driving performance. In this context, the 2008 study from Philip et al. is very interesting.¹³ This involved 38 patients with untreated OSAS and 14 control subjects who were asked perform MWT and also a 90-min test of real driving performance. It was thus shown that patients considered as drowsy (MWT 20–34 min) or very drowsy (MWT < 20 min) made significantly more driving errors than control subjects and patients considered as vigilant (MWT 34–40 min). On the other hand, there was no significant difference between vigilant patients and control subjects. Thus, in France, according to the French sleep medicine society recommendations, a latency of more than 33 min is considered a good alertness, predicting actual safe driving.¹⁶

There are many other tests available for the assessment of sleepiness described in the literature. We will mention only two frequently used tests.

Firstly, Multiple Sleep Latency Tests (MSLT) are used to measure the diurnal tendency to fall asleep and to look for the presence of sleep onset rapid eye movement periods. Here it is very important to understand the difference from MWT: MSLT are used to measure the ability to fall asleep while MWT are used to measure the ability to stay awake, which is a totally different approach.¹¹ The MSLT will be useful when sleepiness is detected in order to try to determine the cause (hypersomnia, narcolepsy, etc.).

The Oxford sleep resistance test is also an interesting test. The principle is globally similar to the MWT, except that instead of the EEG, EOG, and EMG sensors which detect sleepiness, the subject is asked to press a button in response to a light signal about every 3 s, thus revealing sleepiness when there are repeated omissions.⁵ There is a good correlation of this test with MWT. However, it has two major disadvantages: some subjects manage to press the button even when asleep, but above all, there is currently no real consensus on its procedure and interpretation criteria.

Thus, at the present time, MWT seem to remain the best choice for seeking objective sleepiness in a patient with a treated OSAS. Nonetheless, we have seen the residual sleepiness evaluation could also be based on ESS and other tests. That is why we decided to perform a study in order to describe how this evaluation is actually done for aircrew members with OSAS. It could help to propose guidelines in order to have homogeneous management in these cases.

METHOD

In order to study the evaluation of the risk of sleepiness in aircrew members, we decided to perform a retrospective monocentric study with cases of OSAS in aircrew members. The included population was composed of all aircrew members with a history of OSAS seen in our aeromedical center between 2011 and 2018. We decided to exclude cabin crews because of the less important consequences of sleepiness on flight safety in this population.

All files of aircrew members with a mild to severe OSAS and/or a treated OSAS were extracted from our database. Several data were reported: socio-demographic data, flight duty, disease severity, treatment, fitness assessment, and fitness decision. We focused in particular on the residual sleepiness evaluation (ESS, MWT, or others tests) in order to determine its prevalence in this population, and to describe the aeromedical assessment in this context. Aircrew members with residual sleepiness were compared to those without sleepiness in order to find risk factors of sleepiness which could be detected during the aeromedical examination.

This study was approved by a local ethics committee and by the commission on information technology and liberties (Commission Nationale de l'Informatique et des Libertés, CNIL). Quantitative data are described in terms of mean \pm SD and compared with a Student test. Qualitative data are described in terms of percentage \pm SD and compared with a Chisquared test.

RESULTS

Our population is composed of 138 aircrew members (mean age 50.1 ± 9.6 yr, 76.8% civilians, 80.4% pilots). At the time of diagnosis, 60.1% of them were obese; the symptoms described were the following: snoring (66.7%), excessive daytime sleepiness (47.1%), and nocturnal respiratory pauses (15.2%).

Before the diagnosis, ESS was normal (i.e., <11) in 64.9% of cases, with a mean score of 8.5 ± 4.7 . The OSAS was considered severe in 65.4% of cases (otherwise it was moderate) with a mean apnea hypopnea index (AHI) of 36.2 ± 19.2 /h. In addition to lifestyle advice, the treatment was a CPAP in 87% of cases, or a mandibular advancement device in 8.7% of cases.

After the treatment was initiated, the ESS was normal in 93% of cases, with a mean score of 4.2 ± 3.4 , the mean AHI was 4.1 ± 4 , with 87.4% of cases having an AHI <10. Compliance was good, with a mean use of the CPAP of 6.4 ± 1.3 hours/night and 88.2% of nights with the device.

Among our population, 82 aircrew members (59.4%) performed the MWT; all of them were treated with CPAP. This test was normal with no sleep during each 40-min period for 85.4% of them. However, 12 of them had an abnormal test as shown on **Fig. 1**.

We compared those 12 aircrew members to others with normal MWT in order to find risk factors, as showed in **Table I**. We note differences concerning post-treatment ESS (P < 0.01) and compliance (P < 0.01). Nevertheless, 7 aircrew members out of 12 had a normal ESS with an abnormal MWT.

Including 2 aircrew members with an abnormal posttreatment ESS who did not perform MWT, 10.1% of our population (14 aircrew members) had residual excessive sleepiness. After further evaluations in the sleep medicine department, this residual sleepiness was due to a bad tolerance/compliance to CPAP in four cases (28.6%), an associated mood disorder in



Fig. 1. Mean sleep latency in the aircrew members with abnormal MWT.

two cases (14.3%), and was considered sequalae residual sleepiness in seven cases (50%).

After the presentation to the licensing authority or to the military commission, 83.3% of aircrew members were declared fit, with limitations in 96.5% of cases. If the most frequent limitation is a time limitation, 53% of pilots had a multi-pilot limitation.

Concerning the unfit group (16.7% of aircrew members), 43.5% of them were declared unfit because of an associated psychiatric disease, 30.4% because of residual sleepiness, 17.4% because of an associated somatic disease, and two because they did not perform a required test (private pilots who did not want to perform MWT).

DISCUSSION

Thus, among our population, 14 aircrew members (10.1%) had residual sleepiness, which underlines the need for assessing sleepiness in aircrew members with OSAS. This result is

Table I. Comparison Between Aircrew Members with Normal MWT andThose with Abnormal MWT.

	AM WITH MWT < 40 min <i>N</i> = 12	AM WITH MWT = 40 min <i>N</i> = 70	Р
BMI (kg m ⁻²)	31.7 ± 4.6	30.6 ± 5.2	NS
Pretreatment ESS	11.7 ± 4.5	8.3 ± 4.8	NS
Pretreatment ESS > 11 (N , %)	4 (57.1%)	12 (34.3%)	NS
Pretreatment AHI (event/hour)	41.0 ± 23.1	40.3 ± 16.8	NS
Post-Treatment ESS	7.9 ± 5.9	3.4 ± 2.2	< 0.02
Post-Treatment ESS > 11 [<i>N</i> (%)]	5 (41.7%)	0	<0.01
Post-Treatment AHI (event/hour)	4.1 ± 7	3.9 ± 3.5	NS
CPAP Compliance (hours/night)	6.1 ± 1.4	6.4 ± 1.3	NS
CPAP Compliance (% of nights)	86.4 ± 14.6	90.1 ± 9.6	NS
Unsatisfactory CPAP Compliance [<i>N</i> (%)]	4 (30%)	4 (5.7%)	<0.01

MWT = Maintenance of Wakefulness Tests; NS = not significant; BMI = body mass index; ESS = Epworth Sleepiness Score; AHI = Apnea Hypopnea Index; CPAP = continuous positive airway pressure device; unsatisfactory CPAP compliance is defined as a use less than 6 h per night and/or less than 80% of nights. comparable to those of the literature, such as Pepin et al.¹² or Gasa et al.,¹⁰ who found, respectively, 12% and 13% of residual sleepiness in OSAS patients treated with CPAP.

It is interesting to note that the first cause of residual sleepiness in our population is not a defect in the compliance and tolerance of the treatment, as it is in the general population.^{10,15} Indeed, Gasa showed a diminution in the number of hours per night of CPAP use in cases of residual sleepiness (P < 0.0001), which was not seen in our study. However, we must confess that the power of our study with a residual sleepiness group of 14 aircrew members limits these differences.

In aircrew members with cases of treated OSAS, the evaluation of sleepiness is firstly based on the ESS. However, in the case of a normal Epworth score (i.e., less than 11), we cannot be sure of the absence of sleepiness. MWT should then be performed. If these tests return normal, we will consider that there is no sleepiness. Conversely, if the Epworth score is greater than 10 and/or there is an abnormal MWT, there is residual sleepiness that should be explored before discussing the possibility of returning to flying duties.

This procedure for assessing sleepiness therefore seems to be quite easy, as shown on **Fig. 2**. However, this study is a reminder of the difficulty of evaluating sleepiness. As the use of MWT is not mandatory in the regulations, it could be left out of the evaluation. But we have seen mean sleep latency could be very low even with a normal ESS and a satisfactory compliance. So what MWT limit should we choose to affirm the absence of sleepiness among aircrews to protect flight safety?

The study of Philip et al.¹³ described previously did not show any difference in driving performance between control subjects and those with a sleep latency between 34 and 40 min. But this does not mean, in our opinion, that we can declare fit a solo pilot who would have a mean sleep latency of 34 min on four tests. Indeed, this study was performed on a small population and we will probably not have the same level of requirement for a pilot as for another patient.

Thus, the American Academy of Sleep Medicine specifies in its 2005 recommendations that 40-min MWT remain the



Fig. 2. Residual sleepiness screening in aircrew members treated for OSAS.

strongest objective data to assert a person's ability to stay awake.¹¹ In addition, we can read that it is an appropriate expectation for individuals requiring the highest level of safety, which in our opinion includes aircrews.

Another important question in this context is which aircrew members should perform MWT? It does not seem necessary to discuss the interest of these tests in a solo pilot: a complete sleepiness evaluation has to be done.

Is this test necessary for a multipilot, such as an airline pilot? To answer this difficult question, it may be easier to take it the other way around. Are there cases where a pilot would be declared unfit, even in case of multipilot, because of sleepiness on MWT? We have to keep in mind that in our study, five aircrew had an average sleep latency between 0 and 19 min on MWT, with a normal Epworth score for two of them. In particular, there was the case of a 44-yr-old airline pilot with a severe OSAS (apnea hypopnea index = 35/h) treated by CPAP with excellent compliance, a residual apnea hypopnea index at 4/h, and an Epworth score of 8. MWT were performed, showing a mean sleep latency of 11 min on the four tests, i.e., severe sleepiness. The patient was referred to a sleep department and was finally treated with wake-promoting agents. It seems obvious here that such a situation is not compatible with flight safety, even in multipilot. MWT are, therefore, important tests for all pilots with treated OSAS, but also by extension for other specialties (air traffic controllers for example).

In conclusion, the evaluation of residual sleepiness in aircrew with a history of OSAS is an important step in its rehabilitation. This study reminds us that residual sleepiness in aircrew members with OSAS is not rare and that it could be diagnosed even in patients with a normal Epworth score. In this context, MWT are an interesting tool, in association with the Epworth score and the CPAP efficiency and compliance evaluation, to be sure of the absence of sleepiness. From various studies and recommendations on this topic, MWT showing no sleepiness at 40 min seem to be an appropriate expectation to maintain flight safety at a high level. In our opinion, these tests are also necessary even for a multipilot to ensure the absence of severe sleepiness. Finally, it is important to keep in mind that the sleepiness evaluation is only one part of the OSAS evaluation. This condition is a cardiovascular risk factor and should be explored with a complete cardiological evaluation.

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Voluntary Urinary Retention Effects on Cognitive Performance

Cheryl A. Griswold; Kaila A. Vento; Kara J. Blacker

INTRODUCTION: Aircrew in-flight bladder relief remains an understudied stressor; specifically the effects of withholding urination on flight-relevant cognitive performance. This quasi-experimental study investigated whether voluntary urinary retention over a 3-h period negatively impacted cognitive performance.

- **METHODS:** We assessed vigilance using the psychomotor vigilance task (PVT) and measured the P3b event-related potential (ERP) in response to PVT stimuli. We also measured working memory (WM) performance using a change detection task and assessed the contralateral delay activity during the WM task using electroencephalography (EEG). Subjects (*N* = 29) completed a baseline test on both tasks, following bladder voiding and immediately after consuming 0.75 L of water. Subjects performed tasks at 1, 2, and 3 h post-void and urgency to void one's bladder was assessed regularly. A total of 17 subjects were able to complete the entire study protocol. Repeated-measures ANOVAs assessed changes in PVT and WM outcomes.
- **RESULTS:** Reaction time (RT) on the PVT was significantly impaired (5% slower) with longer urinary retention time and showed a 2.5-fold increase in the number of lapses (RT > 500 ms) with increased retention time. Together these results indicate that sustained attention was impaired with increased voluntary urine retention. We did not see significant changes in WM performance with our manipulations. Additionally, neural measures acquired with EEG for both tasks did not show any significant effect.
- **DISCUSSION:** As measured with the PVT, sustained attention was impaired during 3 h of voluntary urinary retention, highlighting the need for further development of adequate bladder relief systems in military aviation.
- **KEYWORDS:** urine retention, cognitive performance, bladder relief, hydration.

Griswold CA, Vento KA, Blacker KJ. Voluntary urinary retention effects on cognitive performance. Aerosp Med Hum Perform. 2023; 94(2):79-85.

ilitary aircrew are faced with numerous operational stressors during flight and an often overlooked area of concern is the lack of adequate bladder relief options, which leads to extended urinary retention. Suppressing the need to urinate during a flight could compromise safety, resulting in operational errors, task saturation, injuries, and potential for mishaps. Personal health can also be negatively impacted by continued urinary retention, including risk of developing urinary incontinence, bladder over-distension, urinary tract infection (UTI), and kidney damage.^{12,17} In fact, over a 14-yr surveillance of the Defense Medical Surveillance System, the occurrence of a UTI reported among U.S. activeduty military pilots and aircrew were 2337 women (56.3%) and 3262 men (4.8%), of which 42% and 10.9% had a recurrence, respectively.¹ While these rates are similar to other occupational communities in the military,¹ the extreme imbalance

between men and women among aircrew makes the relationship less clear. Currently, the effects of a UTI or related urinary infections on aviation-relevant tasks are unknown. However, a UTI (or like infection) could disrupt the aviator's service obligations, grounding them and possibly compromising flight safety.

This issue of urinary retention due to insufficient bladder relief options affects both male and female aircrew. Women are

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most affected because current bladder relief systems are ineffectively designed for a woman's anatomy, creating spills.^{17,20,23} In addition, some external bladder relief systems require the aviator to remove both their aircraft restraint system and their life support equipment, with an additional health and safety hazard if relieved urine is not completely contained. Given the lack of options for bladder relief in the aircraft, incidents could occur where aviators are forced to urinate on the flight line, in their anti-exposure suits, or on the ejection seat following failed attempts to relieve their bladder in flight. Previous work has demonstrated that being underhydrated can negatively impact flight, cognitive, and aerobic performance metrics.^{16,17} For example, pilots who are 3% dehydrated experience a 40% reduction in G tolerance times.¹³ However, little is known about the potential adverse effects of withholding urination for an extended period and how that might threaten an aviator's aeromedical readiness. Therefore, the primary purpose of this study was to determine whether voluntary urinary retention, due to being unable to relieve one's bladder, negatively impacts cognitive performance. Employing a quasiexperimental design, we hypothesized longer durations of urinary retention would increase reaction time (RT) on a psychomotor vigilance task (PVT) and decrease accuracy in change detection on a working memory (WM) task. Repeatedmeasures analysis of variances (ANOVAs) examined PVT and WM over time.

METHOD

Subjects

A total of 29 healthy adults (age: mean = 27.07 yr, SD = 5.18; 15 men, 14 women) participated in this study. The study protocol was approved in advance by the Naval Medical Research Unit Dayton's Institutional Review Board. Each subject provided written informed consent before participating. All subjects self-reported normal or corrected-to-normal vision, no history of psychological, neurological, or medical diagnosis, no known conditions that affect the bladder, no use of tobacco in the past 6 months, and no excessive alcohol use. All participants received a gift card for their contribution to the study.

Materials

For two cognitive tasks, subjects were seated approximately 50 cm from a 15.6-in laptop and stimuli were controlled by MATLAB (The MathWorks, Natick, MA, USA) with Psychophysics Toolbox extensions.⁵ The order of task completion was counterbalanced across subjects.

For the PVT,⁹ subjects were presented with a black uniform background. Periodically, a millisecond counter started to scroll up from zero and subjects had to press the spacebar to stop the counter as quickly as possible. After pressing the spacebar, the counter displayed the achieved RT (in ms) for 1 s, providing the subject with feedback on performance. Interstimulus intervals were distributed randomly from 2 to 10 s and the task lasted for 10 min. The dependent variables of interest for the PVT were median RT and frequency of minor lapses (RT > 500 ms) and major lapses (RT > 1000 ms).

The WM task here was a change detection task modeled after that used by Vogel and colleagues.²⁵ All stimuli were presented on a uniform gray background. Each trial began with a fixation cross for 500 ms, followed by a left or right arrow cue for 200 ms that indicated which hemifield the subject was to attend to. Subjects were instructed to fixate on the cross throughout the entire task. Next, a memory array appeared for 100 ms. In the cued hemifield, subjects saw one of three set sizes presented: two targets, two targets and two distractors, or four targets. The color of targets and distractors (i.e., red and blue) were counterbalanced across subjects. Following the memory array, a 900-ms delay period occurred, followed by a test array. The 2000-ms test array either showed the targets in the cued hemifield in the same positions and orientations (i.e., no change trials) or one target changed position or orientation (i.e., change trials). Subjects responded change or no change for each trial using counterbalanced response keys. Feedback was presented in the form of a color change to the fixation cross for 200 ms: green signaled correct, red signaled incorrect, and blue signaled that a response was not registered. Subjects completed 360 trials per time point (TP), with 120 trials of each set size. The entire task lasted approximately 22 min. The dependent variable of interest was accuracy for each set size separately.

During the cognitive tasks, electroencephalography (EEG) data were recorded continuously from 32 electrodes covering the whole scalp with approximately uniform density using an elastic electrode cap (LiveAmp, Brain Products, Gilching, Germany) with reference electrode FCz in DC mode at a sampling rate of 500 Hz. Electrode impedances for all channels were kept below 10 k Ω . EEG data were processed using the FieldTrip software package.²¹ Details for trial creation, filtering, and averaging are described below for the PVT and WM task data separately. However, artifact rejection procedures for both datasets were identical. Data were rereferenced using a common average reference for the WM data and to electrode Fz for the PVT data. Independent components analysis was performed on epoched data and the eyeblink component was removed. After independent components analysis, EEG waveforms from frontal electrodes (i.e., Fp1, Fp2) were visually inspected to identify voltage fluctuations typical of gross motor movements (amplitude > $\pm 50 \mu$ V). Trials containing these types of artifacts were rejected entirely.

EEG data recorded during the PVT task assessed the P3b component. Data were segmented into epochs of 1500-ms time windows ranging from -500 to 1000 ms from stimulus (i.e., counter) onset. After trial epochs were created, data were bandpass filtered between 0.5–20 Hz. After artifact rejection, the P3b was defined as the most positive going waveform between 250–500 ms post-stimulus onset. Mean amplitude centered around the peak was calculated as the average amplitude \pm 20 ms around the peak.

EEG data recorded during the WM task assessed contralateral delay activity (CDA).²⁵ A band-pass filter of 0.1–30 Hz was used. Then data were segmented into epochs of 3900 ms ranging from -800 to 3100 ms from delay period onset. Any trials containing lateral eye movements were rejected entirely. Finally, CDA was defined as the mean amplitude from 300 to 900 ms during the delay period for contralateral minus ipsilateral posterior electrode sites (O1/O2, P3/P4, P7/P8). CDA amplitude was calculated separately for two targets, two targets and two distractors, and four targets.

To rate void urgency, the Urgency Perception Score was used.² The Urgency Perception Score is a valid and reliable means of grading urgency, ranging from 0 (no urge) to 4 (desperate urge). The scale demonstrates excellent test-retest reliability (intraclass correlation of 0.95) and is validated against clinical interviews.⁷ Subjects provided a rating before and after each cognitive task during each TP and were shown the scale upon each rating, as seen in **Fig. 1**.

To ensure urine is free of most germs and blood for result accuracy, subjects used a "mid-stream clean-catch" technique for urine sample collections (i.e., using a disposable sanitary towelette and urinating 2 s before collecting the sample in a sterile container) for the pre- and post-testing. Urine concentration [i.e., urine specific gravity (USG)] examined hydration status while urine glucose and pH (reagent test strips) examined urinary tract health.

Samples were stored in the refrigerator for a maximum of 7 d. After standing 2–3 h in the laboratory following removal from refrigeration, urine samples were measured at $20 \pm 2^{\circ}$ C (Traceable thermometer, Fischer Scientific, Hampton, NH, USA; $\pm 0.2^{\circ}$ C accuracy) for all hydration assessments.

From the collection container, 20 mL of urine was transferred into a 30-mL test tube. A digital handheld refractometer (Pen-Urine S.G. Refractometer, Atago, Tokyo, Japan) measured USG to assess hydration per the manufacturer's instructions. Duplicate measurements were averaged and, if there was a >0.005 variation between the two measurements, a third measurement was performed using the median. The USG cutoff value of ≥1.020 is considered underhydrated, with higher values risking dehydration.¹⁷

Procedures

In preparation for the visit, subjects were asked not to consume alcohol within 24 h, not to consume caffeine within 12 h, and not to exercise on the morning of the visit. Upon arrival, subjects were asked to void their bladder (void 1), after which baseline anthropometric measurements were taken. Subjects then completed the two cognitive tasks with EEG recording. These initial measurements are henceforth referred to as the baseline TP. After completing baseline measures, the subjects were asked to void their bladder (void 2, baseline) while collecting a urine sample. Next, subjects were asked to drink 0.75 L of water within 15 min. Following the baseline bladder void and water consumption, subjects were regularly assessed via the cognitive tasks and self-report ratings of urgency to void their bladder. Subjects were instructed that when they reached the point where they needed to void their bladder within the next 10 min (i.e., desperate urge) or became too uncomfortable to continue, they would inform the experimenter and the post-protocol completion steps would begin. Cognitive testing with EEG recording and vitals were assessed at 60, 120, and 180 min post-baseline bladder void, hereafter referred to as TP60, TP120, and TP180, respectively. Once the final TP was complete, or if the subject decided to stop, the subject voided their bladder (void 3, post) and provided a urine sample (Fig. 2).

Statistical Analysis

An a priori power calculation determined a sample size of N = 26 (Cohen's F = 0.27, an alpha level of 0.05, and 90% power) coming from a previous study showing the degree of performance impairment during a hypoxia exposure as measured by EEG.⁴ All statistical analyses were conducted using SPSS (version 27, 2020, IBM Corp). Of the 29 subjects who participated, a subsample of 17 subjects (10 men, 7 women) completed the entire data collection period (i.e., testing 180 min post-void). For those 17 subjects, changes in performance were assessed using repeated-measures ANOVAs with TP as a factor with 4 levels: baseline, TP60, TP120, and TP180. However, we also examined paired-samples t-tests for the entire sample of 29, comparing performance measures at baseline compared to the last available time point (i.e., the final measurement before participation was withdrawn to void one's bladder). These analyses yielded the same direction of effect and significance level in every instance and, therefore, we only report the repeated-measures ANOVAs below for brevity. In addition, the Greenhouse-Geisser correction was applied where Mauchly's test showed that the sphericity assumption was violated.



Grade	Definition			
0	No urge (Not at all)			
1	Mild urge (I can delay urination for over an hour if I have to)			
2	Moderate urge (I can delay urination for greater than 10 minutes but less than 60 minutes)			
3	Severe urge (I can delay urination for less than 10 minutes)			
4	Desperate urge (I must urinate immediately)			

Fig. 1. Average urgency to void ratings by time point (TP) and urgency rating scale schematic as shown to subjects. Error bars represent standard error of the mean (SEM).



Fig. 2. Study visit procedures. After EEG preparation, participants completed a baseline time point of the two cognitive tasks, the Psychomotor Vigilance Task (PVT) and Working Memory (WM) tasks. EEG was always recorded during cognitive tasks. Urgency to void one's bladder was reported before and after each cognitive task, represented by the arrows.

RESULTS

To examine changes in subjective urgency ratings across the TPs, we averaged the pre- and post-task ratings for both tasks to create an average urgency rating for each TP. A main effect of TP emerged [*F*(2.101,33.620) = 64.992, *P* < 0.001, η_P^2 = 0.802]. Pairwise comparisons demonstrated that every TP was significantly different from every other, all *P*s < 0.001, with urgency increasing at later TPs (Fig. 1).

To validate the experimental manipulations, a paired-samples t-test on USG demonstrated that subjects were significantly less hydrated (mean = 1.0222 ± 0.0066) at baseline compared to after TP180 (mean = 1.0098 ± 0.0045) [t(16) = 8.712, P < 0.001, d = 2.113]. For PVT median RT, the main effect of TP was significant $[F(3,14) = 2.902, P = 0.044, \eta_P^2 = 0.154]$. Fig. 3A shows that RT increased with longer TPs. Pairwise comparisons specifically demonstrated a significant slowing of RT for TP180 compared to baseline (P = 0.048). For minor lapses, the main effect of TP was also significant [F(3,14) = 3.964, P = 0.013, $\eta_p^2 = 0.199$]. Fig. 3A shows that minor lapses increased in frequency with later TPs. Pairwise comparisons specifically demonstrated that TP60, TP120, and TP180 all had more lapses than baseline, all Ps < 0.05. For major lapses, the main effect of TP did not reach significance [F(1.958,31.322) = 1.442]P = 0.252 (Fig. 3A). To demonstrate the role of urgency to void one's bladder on changes in PVT performance, as opposed to general time on task effects, we tested nonparametric correlations on urgency rating and median RT, as well as minor lapses. There was a significant positive association between urgency to void and median RT [$\rho(97) = 0.241$, P = 0.017] and urgency to void and minor lapses [$\rho(97) = 0.220$, P = 0.030]. Additionally, for P3b amplitude, the main effect of TP was not significant [F(3,14) = 1.110, P = 0.354] (**Fig. 3B**).

For the WM task, each set size was analyzed separately with accuracy as the dependent variable. For two targets, the main effect of TP was not significant [F(1.938,31.002) = 0.224, P = 0.794]. For two targets and two distractors, the main effect

of TP was also not significant [F(3,14) = 0.731, P = 0.539]. Finally, for four targets, the main effect of TP was not significant [F(1.949,31.190) = 0.298, P = 0.739]. **Fig. 3C** illustrates these results. For the CDA amplitude, for two targets, the main effect of TP was not significant [F(3,14) = 1.058, P = 0.376]. For two targets and two distractors, the main effect of TP was not significant [F(1.965,31.436) = 0.775, P = 0.467]. For four targets, the main effect of TP was also not significant [F(3,14) =1.269, P = 0.296]. Results can be seen in **Fig. 3D**.

DISCUSSION

The current study examined the effects of voluntary urinary retention on neurocognitive performance. We found that RT on the PVT was significantly impaired (slower), and subjects also showed a significant increase in the number of minor lapses (RT > 500 ms) with longer urinary retention time. Together these results indicate that sustained attention was impaired with increased voluntary urinary retention. However, we did not see significant changes in WM performance with our manipulations. Additionally, neural measures acquired with EEG for both tasks also did not show any significant effect. The experimental manipulations employed here were mild compared to being unable to void one's bladder during actual extended duration military aviation missions. The RT and attentional lapses in the current study are evidenced in isolation as participants focused on only this one task. However, in an operational environment, multiple tasks and inputs are often co-occurring, which leads to dual- or multitasking. Multitasking has been shown to degrade RT performance, as well.^{5,22} Therefore, slowing responses would likely be exacerbated under both urinary retention and dual- or multitask conditions.

To the best of our knowledge, no previous study has examined the effects of urinary retention on cognitive performance. However, we used the PVT⁹ as one of our primary measures of performance because it is a gold-standard for assessing



Fig. 3. A) Psychomotor Vigilance Task (PVT) performance results across time points. Group average median reaction time (RT) is displayed with the left y-axis and minor and major lapses are shown with the right y-axis. B) P3b mean amplitude results from the PVT task across time points. C) Working Memory (WM) task accuracy results and D) corresponding CDA mean amplitude results, shown by set size for all time points. Error bars represent SEM.

vigilance in the field and has been studied extensively with sleep deprivation,^{6,15,18,26} hypoxia,^{4,11} and other aeromedi-cally relevant performance metrics.^{3,19} As a comparison, our results here showed a 16-ms slowing of RT after 3 h of urinary retention, which is in line with the effects of a blood alcohol level of 0.06%¹⁰ or breathing 10% oxygen.^{4,10} The number of lapses here increased by 2.7 lapses, which exceeds the increase seen after four nights of partial sleep deprivation, a blood alcohol level of 0.08%, or a 10% oxygen hypoxia exposure.¹⁰ Finally, the effects seen here represent a 5% increase in RT, which is comparable to that seen under dual-task conditions, such as walking and performing a cognitive task.²² Therefore, the adverse effects on cognitive performance in an operational setting might be more severe and widespread than witnessed in this controlled environment, though comparable to that of fatigue, alcohol intoxication, and hypoxia. This highlights the degree to which urinary retention could impact operational performance and the need for additional research on the topic.

Here we focused on the effects of urinary retention on cognitive performance, but additional health sequalae of continued

urinary retention are also possible, including development of urinary incontinence, bladder over-distension, UTI, and kidney damage.^{12,17} UTIs are the most prevalent diagnoses among active-duty women and are highly recurrent for pilots and aircrew.¹ To the best of our knowledge, there is no research on the effects of a UTI on cognitive ability. However, more extreme insults to the urinary system, such as kidney failure, has been associated with decreased cognitive function in adults of all ages.¹⁴ Cognitive performance has even been shown to rebound following dialysis or transplantation.⁸ It is known that a UTI (or like infection) disrupts an aviator's service obligations, grounding them and possibly compromising flight safety if flying. For example, the average UTI symptoms for females last 6.1 d, restricting 2.4 d of physical activity, contributing to 1.2 d of absences and 0.4 d in bed.²⁴ Within the military, between 2000-2013, UTIs accounted for a yearly average of 2240 hospital bed days and 4981 d of lost work time.1

The current study also elucidates both the implications of insufficient bladder relief systems for aircrew and provides a better understanding of the performance repercussions of voluntary urinary retention. However, it was not without its limitations. The study's enrolled sample size of 29 was based on a priori power analysis using EEG measures. However, only 17 participants completed the full 3-h intervention, which suggests that our study was likely underpowered. This lack of power may have contributed to our null effects on WM performance and EEG measures of interest. A follow-on effort accounting for attrition is warranted, especially given the understudied nature of the topic. Additionally, a comparable group experiencing acute under hydration is missing. This is important because "tactical dehydration" is used by aviators to circumvent the issue of bladder relief in the aircraft and there are known negative repercussions of dehydration on performance. Instead, this study emphasized urinary retention, rather than hydration status on cognitive performance.¹⁶ Thus, interpretation of results is cautioned. Additionally, sex differences were not examined given the small sample, and we recommend larger powered studies to evaluate cognitive performance and urinary urgency outcomes. Similarly, the effects on sustained attention had no comparison group.

Nevertheless, the current study provides a foundation for future experimental designs that might test the effectiveness of relief systems with a more realistic simulation. For example, prospective studies could conduct a similar intervention examining cognitive performance over 3 h among aviators in full gear in a simulated cockpit, comparing two groups against urinary retention, having 1) refrain from fluids for 12 h (USG > 1.020), unable to consume additional fluids, and 2) well-hydrated (USG < 1.020), able to consume fluids and both able to take bladder relief breaks. Furthermore, future research should examine the additive effects of multiple stressors and how urgency to void one's bladder might interact with operational stressors such as hypoxia, spatial disorientation, fatigue, increased workload, or G forces. To mitigate in-flight bladder relief concerns, we recommend small frequent fluid consumption sips and avoidance of diuretics or foods that stimulate the urge to urinate (such as highly caffeinated or energy drinks).

In conclusion, aircrew in-flight bladder relief systems have not kept pace with increases in mission duration and aviator diversity.^{20,23} We demonstrated that sustained attention was impaired during 3 h of voluntary urinary retention as measured with the PVT. The knowledge gained will help educate aviators on the negative impact of voluntary urinary retention. These data should promote advances in bladder relief systems suitable for all aircrew.

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Abdominal Crunch Syndrome Creates a Diagnostic Challenge in Treating a Pilot with Acute Upper Abdominal Pain

Ameet Kumar; Sumesh Kaistha

BACKGROUND: A diagnosis in acute abdomen may remain elusive especially when the cause is rare. We report this interesting case of a fighter pilot presenting with acute abdominal pain. The case posed significant challenges in reaching the correct diagnosis of abdominal crunch syndrome. The syndrome is rare with only seven reports in the literature so far. To the best of our knowledge, this is the first ever report of this condition in an aircrew. A 37-yr-old pilot presented with severe upper abdominal pain and sweating. During examination, he developed CASE REPORT: bradycardia and was admitted with a presumptive diagnosis of acute coronary syndrome. Investigations revealed no myocardial ischemia on ECG, transaminitis, raised CPK, CKMB, and LDH. A CECT scan of chest and abdomen was normal. A GI surgery consult was sought where we connected the transaminitis and raised CPK and considered the possibility of rhabdomyolysis. On specific inquiry, the aviator gave history of unaccustomed exercise with a vigorous session of abdominal crunches a day prior. Thus, a diagnosis of abdominal crunch syndrome was concluded. The aviator did not associate his vigorous exercise with the occurrence of pain and, therefore, did not mention it. It DISCUSSION: would have avoided unnecessary investigations and delay in treatment. From the aeromedical safety aspect, had the aviator flown on the day he developed pain, there was a possibility of developing severe pain exacerbated by the G force and G suit and sudden in-flight incapacitation. From the perspective of the aircrew, it is advisable that they avoid sudden, unaccustomed exercise.

KEYWORDS: acute abdomen, pilot, exertional rhabdomyolysis, rectus abdominis syndrome, aeromedical safety, in-flight incapacitation.

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Patients presenting with upper abdominal pain is one of the commonest emergencies presenting to the emergency department. The diagnosis is often surgical and sometimes medical and usually both specialties are involved in the evaluation of such patients. The surgical conditions could range from biliary colic or acute cholecystitis to peptic perforation and even aortic dissection. The medical conditions could be acid peptic disease or hepatitis to the more sinister pancreatitis or even inferior wall myocardial infarction. Thus, the evaluation of such patients, usually, proceeds in these directions. There are other uncommon causes of upper abdominal pain and, in such cases, there is usually additional time taken before a definitive diagnosis can be arrived at. An abdominal wall condition leading to upper abdominal pain is exceedingly rare and is not entertained as a possibility, upfront, in the initial evaluation. We report this

interesting case of a fighter pilot presenting with acute upper abdominal pain which perplexed many clinicians before making the right diagnosis of abdominal crunch syndrome.

CASE REPORT

A 37-yr-old fighter pilot presented with a history of severe upper abdominal pain with sweating of 12 h duration which

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was sudden in onset following intake of food. He denied any history of fever, nausea or vomiting, melena or hematemesis, jaundice, prodromal symptoms, or bowel or bladder symptoms. He denied any history of dark colored urine. He had not consumed alcohol in the last 72 h and denied any flying related stress. Clinically, he was afebrile with a pulse rate of 64/min which fell to 36/min on admission but was normotensive. He had no pallor, cyanosis, pedal edema, or icterus. Abdominal examination revealed tenderness in the epigastric region with guarding but no rigidity.

He was admitted to ICCU with a provisional diagnosis of acute coronary syndrome. A troponin T test was negative; ECG showed sinus bradycardia, but no evidence of myocardial ischemia and the 2-D Echo was normal. His blood investigations showed normal hemogram, deranged LFT [total bilirubin 1.8 mg \cdot dL⁻¹ and direct bilirubin 0.2 mg \cdot dL⁻¹, aspartate transaminase 542 U \cdot L⁻¹ (normal, 0–40); alanine transaminase 453 U · L⁻¹ (normal, 0-40), alkaline phosphatase 42 U \cdot L⁻¹, and high CKMB 218 U \cdot L⁻¹ (normal, <190), CPK 1312 U \cdot L⁻¹ (normal, <25), and LDH 918 U \cdot L⁻¹ (normal, 225–450)]. His serum amylase was 36 U \cdot L⁻¹, blood urea nitrogen was 19, serum creatinine was 1.0 mg \cdot dL⁻¹, and serum sodium and potassium were 140 and 4.4 meq \cdot L⁻¹, respectively. At this time, the differential diagnoses considered were acute pulmonary thromboembolism, acute viral hepatitis, acute pancreatitis, mesenteric ischemia, acute intermittent porphyria, and hemolytic anemia. A medical gastroenterology consult was sought.

CT angiogram of chest and abdomen was done which ruled out pulmonary thromboembolism, acute pancreatitis, and mesenteric ischemia. Urine for porphobilinogen was negative. Viral markers were negative for acute viral hepatitis. Peripheral blood smear did not show any evidence of hemolysis and the hemoglobin electrophoresis and sickling test were negative for sickle cell trait. Test for G6PD deficiency was also negative. An upper GI endoscopy was normal.

With the diagnosis being elusive, a gastrointestinal surgery consult was sought on day 3 of admission. The entire history, clinical findings, and investigations were reviewed along with the patient. The raised CK, LDH, and transaminitis caught our attention. Further, the CKMB/CK relative index was less than 3, which indicated a skeletal muscle source. This was the tipping point which prompted us to take history of any unaccustomed exercise and the pilot confirmed that he had restarted exercises after a 3-mo break and had a vigorous session of abdominal crunches for 20 min a day prior to the onset of pain. But as he did not consider it significant, he did not bring it out in the initial history giving.

Based on the above, a diagnosis of exercise-induced abdominal wall rhabdomyolysis (abdominal crunch syndrome) was made. All cardiac medications were stopped and he was treated with hydration, analgesics, and rest. He recovered rapidly thereafter with progressively decreasing CK and transaminases levels and was discharged on day 5 of his admission. He was reviewed after 10 d when he had no complaints, his examination was unremarkable, and all his biochemical parameters had normalized. He was returned straight to active flying thereafter without subjecting him to any period of observation.

DISCUSSION

Exertional rhabdomyolysis (ER) is a well described condition following sudden and unaccustomed exercise. However, its presentation as upper abdominal pain has been rarely reported. Abdominal crunch induced rhabdomyolysis was first reported by Schmitt in 1983,¹² who termed it 'rectus abdominis syndrome' and there are only seven reports of it in the literature so far (**Table I**). To the best of our knowledge, this is the first ever report of this condition in an aircrew.

ER, in general, has usually been reported in military and paramilitary personnel because of the prolonged and intense physical activities undertaken, often in hot weather conditions and in military uniform. However, there are increasing reports of this condition in the civil population too. There is a paucity of data from Indian populations on ER, but data exists from western populations. Among civil populations, one study found a 5% incidence of ER among all cases of rhabdomyolysis. Two more studies reported 21 cases in 13 yr and 89 cases in 12 yr, respectively. Both studies were prompt to point out the majority of these cases occurred in the latter half of the study period and attributed it to increasing popularity of high-intensity work outs in the gym.⁵ The incidence of ER has been found to vary between 0.3% in one group of marine recruits to 3% in a group of army officer candidates.^{1,11} A Mayo Clinic study reported 20 times more incidence of ER in military personnel as compared to civilian cases.¹¹ One study showed that the occurrence of ER after severe exercise depended on the levels of preconditioning in variously trained healthy volunteers.⁸ The study also showed that ER occurred earlier in the training period and was a function of the how well or less trained an individual was. It is postulated that the intense physical exertion leads to the exhaustion of the ATP molecules of the skeletal muscle cells, which drives dysfunction in the muscle cell membranes, thereby causing rhabdomyolysis.²

Acute abdomen is a Pandora's box with many differential diagnoses and, at times, it takes time and more investigations to come to a diagnosis. But the cornerstone of approach will remain meticulous history taking and clinical examination. The aviator did not associate his vigorous abdominal crunches with the occurrence of pain and did not mention it. If the history had been forthcoming in the initial evaluation, a lot of unnecessary investigations would have been avoided. Had it not been elicited later, it would have led to more investigations and probably the condition would have gone undiagnosed and could have led to a period of observation for him before he could be returned to flying. It would be pertinent to note that had the ER been severe, any further delay in diagnosis could have worsened his condition, possibly progressing to serious complications like acute kidney injury or disseminated intravascular coagulation.

Table I. Summary of All Cases of Abdominal Crunch Syndrome Reported in the Literature.

		AGE/	PRESENTING	INCITING	CK LEVELS	CKMB/CK	AST/ ALT	LDH	
YEAR	AUTHOR	SEX	COMPLAINT	ACTIVITY	(U/L)	RELATIVE INDEX	(U/L)	(U/L)	OUTCOME
1983	Schmitt ¹²	19/M	Acute abdominal pain	Intensive body building exercises	22,388	0.1	90/35	973	Recovered well
1992	Reimers ¹⁰	21/F	Acute abdominal pain	Ski gymnastics and sit ups	7800	CKMB value N/A	-	-	Recovered well
		18/M	Acute abdominal pain	Abdominal muscle training	13,860	CKMB value N/A	-	-	Recovering well, lost to follow-up
		20/M	Acute abdominal pain	Swimming and alcohol binge	17,500	CKMB value N/A	-	-	Recovered well
1998	Kao ⁷	29/m	Anterior abdominal wall muscle pain	Vigorous sit ups for the past 5 d	12,586	0	-	149	Recovered well
1999	Haas ⁶	23/M	Right upper quadrant abdominal pain	Abdominal crunches	53,000	CKMB value N/A	568/200	1294	Recovered well
2003	Dai ³	-	-	-	-	-			-
2008	Chawla ¹	24/M	Abdominal pain and nausea	Abdominal crunches along with alcohol binge	29,536	CKMB value N/A	174/40	974	Recovered well
2018	Echague ⁴	27/F	Abdominal pain and swelling over mons pubis	Intense powerlifting	5917	CKMB value N/A	221/176	-	Recovered well
2022	Present case	37/M	Severe upper abdominal pain and sweating	Abdominal crunches	1312	0.17	542/453	918	Recovered well

N/A: Not available.

Clinical diagnosis centers on history of intense physical activity with complaints of myalgia in the affected group of muscles and dark colored urine that is caused by myoglobinuria. Myoglobinuria is seen in about 50% of cases only.⁴ Apart from meticulous history taking and examination, the lynchpin for the diagnosis of ER is elevated CPK and low CKMB/CPK ratio. Many studies have shown that ER is associated with transaminitis and the origin, which is myocytes rather than hepatocytes (Table I).⁹ Our patient too had transaminitis, apart from elevated CPK and LDH, which also pointed toward ER.

Notably, our case did not have dark colored urine. Probably the extent of ER was not enough to cause significant myoglobinuria. It is estimated that at least 100 g of muscle needs to be injured to produce a myoglobin level >25 μ g \cdot ml⁻¹ and which is the minimum level to color the urine dark brown or red.² Retrospectively, the severity of ER in our case was not severe and, consequently, he recovered quickly without requiring any major intervention except for hydration and analgesia with rest. Severe cases of rhabdomyolysis can result in fever, hypotension, confusion/delirium, acute kidney injury, metabolic acidosis, and dyselectrolytemia leading to life threatening arrhythmias. Treatment in these cases includes rapid hydration, mannitol administration, alkalinization of urine, correction of dyselectrolytemia, and emergency dialysis. Fasciotomy is done if compartment syndrome occurs. Schmitt has termed this crunch-induced ER as rectus abdominis syndrome because the rectus abdominis is enclosed in a tight fascial compartment that provides little room for expansion of the muscle swelling caused by the intense exertion.¹² Thus, if the ER was severe, probably a fasciotomy might have been indicated.

If a history of unusual physical activity had not been forthcoming, the case would have been investigated for other causes of rhabdomyolysis, which includes alcohol, drug abuse (opiates, benzodiazepines, amphetamines, and recreational drugs like 'ecstasy'), therapeutic drugs (corticosteroids, salicylates, statins, etc.), sickle cell crisis, metabolic myopathies (e.g., McArdles disease), or muscular dystrophies (e.g., Duchenne and Becker dystrophies). In the latter two conditions, muscle biopsy with immunohistochemical studies is indicated. However, our patient did not have a history suggestive of rhabdomyolysis in the past and did not suffer from similar episodes during his follow-up period. Thus, further investigation was not warranted in our case.

From the aeromedical safety aspect, it is pertinent to highlight that had the aviator flown on the morning of the day he developed abdominal pain, he would have developed this pain during his sortie. When he would have pulled high G, the G suit would have only further increased the compartmental pressure of the rectus abdominis, causing worsening of pain and resulting in sudden in-flight incapacitation.

This article underscores the importance of thorough history taking with a good clinical examination and scrutiny of all investigations ordered to pick up rarer causes of acute abdomen. ER or abdominal crunch syndrome, although rare, should be kept in the differential in any patient presenting with an acute abdomen. This will prevent a misdiagnosis, unnecessary investigations, and worsening of the condition for the want of a definitive diagnosis. From the perspective of the aircrew, it is advisable that they avoid sudden, unaccustomed exercise and resort to graded escalation of the severity of physical training.

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Pharmacological Relief of Acute Urinary Retention in a Remote Environment

Jennifer Law; Vanessa Cardy

BACKGROUND: In spaceflight, acute urinary retention (AUR) could develop as a sequela of medication use, urinary tract infection, urolithiasis, or intentional urine holding. While AUR is generally treated with bladder decompression, urinary catheterization could be difficult operationally in terms of training and proficiency, supplies, and lack of space or privacy. This report discusses a case in which tamsulosin and lorazepam were used successfully on an offshore ship while awaiting medical evacuation, a situation that could arise in remote locations where aerospace operations are conducted.

- **CASE REPORT:** A 52-yr-old man with hypertension and obstructive sleep apnea but no formal diagnosis of benign prostatic hyperplasia was unable to urinate for over 16 h while on a deep-sea fishing vessel approximately 200 nmi offshore. By phone, the physician providing remote medical direction diagnosed AUR in the setting of possible infection and prescribed acetaminophen, ciprofloxacin, and a trial of tamsulosin as the ship did not have any medical personnel trained to perform urinary catheterization and there were no catheter supplies available. Lorazepam was later added for anxiolysis and potential smooth muscle relaxation. Within 1 h of initial medication administration, the patient successfully voided a large quantity of urine, which tested positive for infection by urine dipstick. The patient was continued on antibiotics and evacuated to a medical facility onshore for further management.
- **DISCUSSION:** Pharmacological treatment could be considered as a temporizing measure where operational constraints limit the ability to perform urinary catheterization to relieve acute urinary retention.
- **KEYWORDS:** tamulosin, benzodiazepine, spaceflight, urinary retention, wilderness medicine.

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cute urinary retention (AUR) is a known medical condition in spaceflight. Possible causes include medications, psychosocial related to intentional delay in voidingdue to schedule and toilet access, and lack of a gravity vector.⁹ In particular, antiemetics routinely used for preventing and treating space and entry motion sickness are known anticholinergics, which predispose otherwise healthy astronauts to urinary retention.

Stepaniak et al.¹³ detailed the clinical course of a Shuttle crewmember with no prior urinary history who developed recurrent AUR on two separate missions both in flight and postflight, requiring multiple urinary catheterizations. On the first flight, only one urinary catheter was available onboard, requiring the crewmember to clean it as well as possible in between intermittent catheterizations or voiding trials during indwelling catheterization. Despite antibiotic prophylaxis with nitrofurantoin and subsequently trimethoprim/ sulfamethoxazole, when the onboard supply of the former medication was depleted, an in-flight urine dipstick was positive for leukocytes and postflight urine culture was positive for trimethoprim/sulfamethoxazole-resistant *E. coli*. On the second flight, the crewmember again needed to self-catheterize on flight days 1 and 2, but was able to void spontaneously until immediately after landing, at which time he developed AUR requiring catheter insertion by a flight surgeon. Urinalysis was positive for infection. The cause of this crewmember's AUR was

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likely multifactorial and his use of both promethazine and scopolamine to treat space motion sickness symptoms was thought to predispose him to AUR.

More recently, a review of in-flight and postflight records from Mercury, Gemini, Apollo, Mir, Shuttle, and International Space Station Expeditions 1–38 found 9 documented cases of AUR and 16 total if symptoms suggestive of urinary retention (bladder fullness/pressure, difficulty initiating/hesitancy) were also included.³ If a crewmember took promethazine, the odds of developing AUR were three times higher. Women were four times more likely than men to develop AUR. Even with antibiotic prophylaxis, the infection rate of urinary catheterization was 42%, and a catheterized crewmember was 2.5 times more likely to have a urinary tract infection (UTI), although the incidence was too low for this to be statistically significant and it was unclear whether the UTI preceded or was caused by AUR.

These cases demonstrate that AUR is a concern for spaceflight and urinary catheterization—the standard of care for treating AUR—is not a benign procedure. Furthermore, urinary catheterization has significant limitations in the operational setting. The ability to perform the procedure requires training and maintenance of proficiency, plus adequate supplies, including disinfection swabs, lubricant, catheters, and collection devices. An environment that allows privacy and the ability for the patient to lie flat is needed, which can be complicated by microgravity or on aircraft ferrying a postflight crewmember. Moreover, the procedure could be time-consuming unless the provider is very experienced, thus negatively impacting tight operational schedules.

Given these challenges, being able to treat AUR pharmacologically would be ideal, not only in spaceflight but also in remote environments that have similar constraints. This report describes a case in which tamsulosin and lorazepam were used successfully to relieve AUR in an offshore fisherman awaiting medical evacuation, a case study that could be applied to aerospace operations.

CASE REPORT

A physician providing remote medical direction to a deep-sea fishing vessel received a phone call about a 52-yr-old man with hypertension and obstructive sleep apnea who had not been able to urinate since the night prior. He was only on ramipril daily and used a continuous positive airway pressure (CPAP) machine at night. He had a 2-yr history of nocturia and decreased urinary stream, but had never consulted for this issue. He had no known drug allergies. He was in his usual state of health at dinnertime the night before the call came in, when he noticed mild dysuria without any urinary frequency, urgency, sense of incomplete bladder emptying, or hematuria. He had no localized redness or itching. There was no history of trauma and he denied any history of new sexual contacts before getting on the boat 10 d prior or since boarding.

The dysuria recurred at 21:30 when he voided before going to sleep and then, at 03:00, he was awoken and kept awake by

the sensation of needing to void. This sensation intensified throughout the morning and he could not urinate despite efforts to relax or drink copious amounts of liquids. He took acetaminophen at 05:00 without relief. He was unable to do his morning shift and finally notified his captain at 13:00, at which time the remote physician was called. At this point it had been 16 h since his last urination.

By phone with the captain as an intermediary, the remote physician obtained more history and ascertained the patient had no fevers or chills, flank pain, back pain, chest pain, cough, myalgias, or shortness of breath. He had not vomited but was beginning to feel nauseated. The captain reported that the patient appeared to be pale, sweaty, and in pain. He was talking quietly and trying not to move. His vital signs were: blood pressure 189/96, pulse 110, RR 22. He was afebrile. Under the physician's direction, the captain palpated the patient's abdomen, which was soft above the umbilicus but noticeably tender below it.

Presuming a diagnosis of acute urinary retention in the setting of possible urinary tract infection or prostatitis, the remote physician requested that the ship be turned back to shore to enable a helicopter or rescue boat to medically evacuate the patient. At the time, the fishing vessel, which had neither the supplies for urinary catheterization nor personnel trained to perform such procedure, was 200 nmi from shore off the coast of Newfoundland and had planned to spend another 7–8 d at sea. The remote physician decided that medical evacuation was necessary, not only to decompress the bladder, but also to diagnose and treat the underlying cause. Given the risk of recurrence, the patient could not remain on the ship and sail even further from shore.

In the meantime, the remote physician reviewed the list of medications available onboard. She prescribed oral acetaminophen 1 g since the patient was in significant discomfort, ciprofloxacin 500 mg for possible infection, and a trial of tamsulosin 0.8 mg. The physician opted for adding in tamsulosin because of the 2-yr history of nocturia and decreased stream strength suggestive of benign prostatic hyperplasia, in addition to the possibility that tamsulosin could help the passage of a stone if that were indeed the cause of the blockage. The latter seemed an unlikely cause of complete obstruction, but the relative risk of tamsulosin administration and possible side effects were far outweighed by the risk of prolonged urinary obstruction.

Approximately 35 min after the first call, the ship's captain called back to report that the medications had not been effective and the patient was beginning to be more anxious. A repeat set of vital signs was taken: blood pressure 180/95, pulse 118, RR 24–26. He remained afebrile with normal oxygen saturation. Medevac had been called and the helicopter would arrive in approximately 2 h.

While it was not surprising that the tamsulosin had not yet taken effect, given the patient's worsening anxiety and with the hopes of achieving some degree of smooth muscle relaxation, the remote physician prescribed lorazepam 1 mg. Morphine sulfate was considered for pain relief and smooth muscle relaxation, but given the patient's large body habitus and history of obstructive sleep apnea, the remote physician felt the risk of apnea outweighed potential benefits. The remote physician also began putting together a step-by-step procedure for talking the captain through a suprapubic aspiration using materials available onboard if this became a necessity.

The captain called and reported that the patient had voided a very large amount of urine 20 min after the lorazepam administration and was feeling significantly better. A urine dipstick showed 3+ leukocyte esterase, positive nitrite, and 2+ blood. Ciprofloxacin was continued as treatment for the presumed UTI. Later the patient was successfully evacuated by helicopter and treated at an onshore medical facility.

DISCUSSION

This case illustrated a typical presentation of acute urinary retention and limitations in resources and trained personnel in a remote environment. Since urinary catheterization was not available, pharmacological treatment was attempted and successfully relieved the patient's AUR. In this case, tamsulosin and lorazepam were used.

Tamsulosin is an adrenergic alpha-1A antagonist that is commonly used to treat benign prostatic hyperplasia, in addition to off-label uses for treating bladder outlet obstruction in males and expulsion of ureteral stones. Mechanistically, it works by relaxing smooth muscle in the prostate, which leads to relaxation of smooth muscle in the bladder neck, with a timeto-peak of 4–5 h when fasting and 6–7 h with food.⁶ Older populations may metabolize tamsulosin at a slower rate. In women, tamsulosin has been shown to cause significant relaxation of the urethra¹² and improve voiding difficulty, especially in those with bladder outlet obstruction.²

Benzodiazepines such as lorazepam are typically used to treat anxiety, seizures, and other central nervous system disorders by binding to gamma-aminobutyric acid (GABA) receptors, with a time to peak of 2 h.4 Since GABA receptors are also found in peripheral tissues, including the urinary bladder,¹⁰ it is plausible that a benzodiazepine could be used to relieve AUR. In fact, gynecological textbooks have historically described the use of benzodiazepines for urinary retention.⁸ However, separate randomized controlled trials showed three different benzodiazepines had no apparent benefit in reducing postoperative urinary retention.^{1,7,8} It is worth pointing out the cause of postoperative urinary retention is multifactorial, with many possible confounders,8 and it is unknown whether the results of those studies could be generalized to AUR outside of the operating room setting. In this case, another potential confounder is the patient being on ramipril for unknown duration; there is some evidence that angiotensin-converting enzyme inhibitors can contribute to UTI and potentially AUR within the first month of initiation.¹¹

Morphine was considered by the remote physician for its smooth muscle relaxation properties, but ruled out due to the possibility of respiratory depression in a higher risk patient. Perhaps just as well: urinary retention is listed as a potential adverse reaction to morphine,⁵ so its use could have worsened the AUR.

In this case, the timing of events suggested that lorazepam was associated with relief of the patient's AUR, perhaps in synergy with tamsulosin, which was starting to take effect. Unfortunately, given the nature of the remote consultation and the authors' inability to follow up with the patient, one cannot know for sure whether the medications were directly responsible. More research could help elucidate the effect of tamsulosin alone versus in combination with another drug.

Still, this case raises the possibility that AUR could be treated pharmacologically in a remote environment where operationally it is challenging to perform urinary catheterization, at least as a temporizing measure while arrangements are made to decompress the bladder in a more optimal setting. It would be worthwhile to include tamsulosin in one's field medical kit, since it has a relatively safe profile and can also be used to treat urolithiasis. Given conflicting information about the benefit of benzodiazepines and morphine, and more importantly due to the challenges of carrying controlled substances in the field and at times across international borders, the flight surgeon should carefully consider whether those medications should be included.

Other "tricks of the trade" that have been used by physicians to help their patients with AUR include playing sounds of running water or placement into a warm bath. The latter, of course, would not be feasible in the field or on orbit, but the same idea could be applied by placing a warm, wet towel on the patient's body to stimulate the urge to urinate.

In summary, this report described a case of acute urinary retention in an offshore fisherman, who successfully voided after a trial of tamsulosin followed by lorazepam while awaiting medical evacuation since urinary catheterization was not possible due to the limitations of the remote environment he was in. For spaceflight, which is known to predispose astronauts to urinary retention due to a number of factors, a trial of tamsulosin can be considered and may obviate the need to perform urinary catheterization in suboptimal settings.

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Letter to the Editor re: In-Flight Medical Emergencies Management by Anesthetist-Intensivists and Emergency Physicians

Dear Editor:

We read Diop et al.'s² article with great interest since we have worked on this issue for many years. The authors may be interested to read the article by Chatfield et al. on 'Cross-Sectional Survey of Physicians on Providing Volunteer Care for In-Flight Medical Events' which found similar results as their survey.¹

We fully agree with the authors' statement that "It would, therefore, be helpful for any physician to understand the physiological changes induced by altitude, be aware of the main IME encountered during a commercial flight, and also which medical and human resources are available on board to deal with those." The Aerospace Medical Association (AsMA) has written to several medical colleges encouraging the inclusion of basic aviation medicine training in medical curricula, but with little apparent effect. In April 2020, the President of the Aerospace Medical Association wrote "Most clinicians remain woefully underprepared to advise or even discuss these potential impacts with their traveling patients."⁴ Since more and more people are flying, the great majority of physicians will be asked by some of their patients whether they are fit to fly or not. Since most physicians travel by airplane from time to time, the chance of them being involved in an in-flight medical event is indeed significant, as indicated in your paper.

Allow us to make a few suggestions for clarification. As there is no internationally agreed definition of an 'in-flight medical emergency' as opposed to an 'in-flight medical event', we believe that, for consistency, it is better to refer to 'in-flight medical events', which can be more easily compared from paper to paper regardless of the severity of the event.

In Table I, the question starting 'At cruising altitude...', should be replaced by 'At cabin altitude during the cruise phase of the flight'. Cabin altitude is the critical factor as far as passengers are concerned regardless of the aircraft cruising altitude. For the same reason, the word 'cabins' in the sentence 'Commercial aircraft cabins cruise at an altitude....' in the

second paragraph of page 635 should be removed because the cabin is not cruising at those altitudes (as is explained later in the paragraph).

Also in Table I, the answer that dehydration is higher than at sea level maybe misleading. While it is true that the air is generally dry in an aircraft cabin, with effects such as dry skin and dry mucosa, there is little supporting data that there is a core dehydration. The only article we are aware of addressing this issue scientifically concludes that there is no core dehydration if the passenger maintains a normal intake of fluid.⁵

In Table II, the statement that 'A ground medical assistant is available 24 h a day' is incorrect. While it is true that many airlines have medical ground support available, not all commercial airlines provide that service.

In the third paragraph, page 635, regarding an increase in the volume of gases with decreased pressure, the authors state 'It may be responsible for specific benign symptoms such as abdominal, ear, or sinus pain.' While this is true, we believe it should also be mentioned that some symptoms could be severe, e.g., if a patient was to fly with a bowel occlusion or semiocclusion (which are contraindications to travel by aircraft). From personal experience, not all physicians—including some gastroenterologists—are familiar with this.

In the fourth paragraph, the authors state '…high altitude exposure leads to a decreased stroke volume,…'. The author of the chapter on hypoxia and hyperventilation in the latest edition of "Ernsting's Aviation and Space Medicine"³ states (in the section on general cardiovascular changes with increased altitude) 'Since stroke volume remains essentially unchanged as the heart rate increases,…'.

In the sixth paragraph, the statement 'The U.S. Federal Aviation Administration requires that all planes traveling to or from the United States carry an AED on board,....' is incorrect. The authors reference Hinkelbein, who had referenced

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Mahony, who had misinterpreted the regulation. That regulation only applies to U.S. registered aircraft.⁷ The authors may be interested to read our paper, 'Medical Events on Board Aircraft: Reducing Confusion and Misinterpretation in the Scientific Literature,⁶ where we described many cases of mis-references, misinterpretation, or misunderstanding of aviation medicine principles, with the same aim as the authors' paper—to support improved basic training in altitude physiology and management of medical events on board commercial aircraft.

Finally, regarding complementary help and/or training for those involved in an in-flight medical event, we would like to recommend the application 'AirRx', which is available free of charge in the Apple Store. It provides basic information on altitude physiology, most frequent diagnoses, medications, and equipment, medical legal aspects, and documentation. We would also recommend the publication 'Managing in-flight medical events' on the AsMA website at http://www.asma.org/ publications/medical-publications-for-airline-travel/managingin-flight-medical-events.

The authors suggest didactic online training courses. As they are writing from France, they may be interested to know that La Fédération des Médecins Spécialistes du Québec (FMSQ) offers such a program to its members (en Français).

One of the challenges of management of in-flight medical events is to combine the expertise of specialists working in different fields (such as that of the group surveyed in this paper) to that of medical specialists involved in aerospace medicine.

In Response:

We read with great interest the comments of Dr. Thibeault and Dr. Evans regarding our recent article³ published in *Aerospace Medicine and Human Performance* and we thank them for the quality of their remarks. However, we want to clarify some issues raised in their letter.

We used the terminology of in-flight medical emergency because we primarily addressed the questionnaire to emergency and anesthetist-intensivist physicians. As the goal of our study was to question physicians about their knowledge when potential life-threatening situations arise and not to report the incidence of in-flight medical events or emergency, we believe that the terminology we used was accurate.

As pointed out in the letter, objective data on hydration state during commercial flight are scarce. Some studies found that air travel is associated with an increase of blood osmolality (reflecting pure water losses) and a reduction of plasma volume.^{2,10} Equally, prolonged immobilization during air travel is associated with edema formation in the lower limbs, demonstrating fluid shift from the plasma to the interstitium and leading to plasma volume depletion.^{6,9} Furthermore, in Should the authors wish to develop their ideas on promotion of aeromedical principles to the general medical community, we can suggest contacts in aeromedicine that could assist in this goal (which we fully support).

Claude Thibeault, M.D., and Anthony Evans, M.B.Ch.B.

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this environment people are exposed to low humidity and hypobaric hypoxia. To some extent, this is a similar state to that found at high altitude (e.g., during mountain ascent), where physiological changes have been extensively studied. Acute hypobaric hypoxia increases renal water and sodium ion excretion rates through a decrease of aldosterone and an increase of atrial natriuretic peptide release.^{1,5,7} After days, total body water and plasma volume significantly decrease due to several mechanisms (lower humidity, decrease in vasopressin sensitivity to plasma osmolarity change, increase of respiratory and urine losses, and decrease of water intake linked to thirst dysregulation).^{1,7} Although these findings concern people exposed to the high altitude environment and not specifically people traveling on a commercial flight, we could reasonably assume that the exposure to hypobaric hypoxia during long-haul flight increases the risk of dehydration. In their letter the authors state: "there is no core dehydration if the passenger maintains a normal intake of fluid." It emphasizes the importance of ensuring an adequate fluid intake during commercial air travel, even more so in vulnerable populations (e.g., elderly people), who are more at risk of thirst dysregulation and specific data are lacking to presume

that all passengers maintain a normal fluid intake.⁸ So it seems necessary to focus on dehydration risk during commercial flight and to adopt all necessary mean to prevent it (free water access during the flight, limits on the consumption of diuretic beverages, passenger information). Incidentally, aircrew members are more prone to renal stone disease compared to the general population, probably due to dehydration related to lower fluid intake.⁴

Regarding the necessity of carrying an AED on board, the U.S. Code of Federal Regulations title 14, part 121, states in the section "Emergency Medical Equipment and Training", sub section "Applicability": "this subpart prescribes medical equipment and training requirement applicable to all certificate holders operating passenger-carrying airplanes..."¹¹ As there is no explicit mention that this part concerns only U.S. registered planes, it led us to misinterpret the regulation. Fortunately, it does not alter the main message, which is an automatic external defibrillator is not mandatory on all commercial air flights.

We express our gratitude to Dr. Thibeault and Dr. Evans for their comments and their advice. We share the common objective of promoting knowledge and basic training in aviation medicine to the whole medical community. We wish to develop short didactic training course for all physicians interested, as is already proposed in Quebec, and, in the future, we will be glad to benefit from their expertise and contact in the field of aerospace medicine.

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Aerospace Medicine Clinic

This article was prepared by Jason Burchett, D.O., M.P.H.

Wou're the flight surgeon at an F-16 base when a 37-yr-old male experienced command pilot presents with palpations and chest discomfort, on and off for the last week. He reports this has been a problem since he was a child. He denies any history of syncope, shortness of breath, or exercise intolerance and has never had any problems performing as an F-16 pilot. He also reports excellent $+G_z$ tolerance in the past and his resting heart rate in clinic is 55 bpm. He has an electrocardiogram done in the clinic that is normal; however, a 7-d Holter monitor shows paroxysmal atrial fibrillation (A-fib). He is referred to Cardiology and an echocardiogram is done that shows normal structure and function; he then undergoes pulmonary vein isolation A-fib cardiac ablation.

- 1. What is the long-term recurrence rate of paroxysmal A-fib following this pilot's first pulmonary vein isolation ablation?
 - A. 0–20%.
 - B. 20–40%.
 - С. 40-60%.
 - D. 60-80%.

ANSWER/DISCUSSION

1. B. This pilot has nonvalvular paroxysmal A-fib. Recurrence of A-fib after a single ablation is relatively high. In a 2013 meta-analysis, the success rate of a single cardiac ablation for paroxysmal A-fib was 67% at 1 yr and 54% at 3-5 yr.³ This success rate has traditionally resulted in permanent disqualification of pilots to fly high-performance aircraft after a diagnosis of A-fib with or without cardiac ablation. Indications for cardiac ablation are the presence of symptoms associated with A-fib, typically after ineffectiveness or intolerance of medication.⁷ The pilot in this case was a candidate for ablation therapy since he was symptomatic and unable to tolerate rate control medications like beta blockers due to his low resting heart rate. There is no recommendation to pursue cardiac ablation just to get a pilot back in the air, and appropriate treatment of the medical condition is critical. Some identified risk factors for recurrence of A-fib post ablation include older age, hypertension,

structural heart disease, male sex, persistent A-fib, and presence of coronary artery disease. Early recurrence in the first 1–3 mo post ablation of A-fib can occur in 30–70% of individuals who undergo cardiac ablation; however, this is thought to be due to remodeling and inflammation and may be transient in some cases. That being said, early recurrence is a strong independent predictor of long-term recurrence.⁹ After the early recurrence period, most recurrences are reported in the first 3–6 mo; thus, it is recommended to wait at least 4–6 mo before a return to flying.^{4,12}

After the ablation, the pilot is treated with metoprolol succinate 25 mg daily as well as apixaban 5 mg twice a day for 1 wk. He denied any additional palpations or chest discomfort and had a normal 7-d Holter monitor. He has no history of hypertension, chronic heart failure, vascular disease, diabetes mellitus, stroke, bleeding tendencies, or alcohol use. He has normal kidney and liver function and takes no medications.

- 2. What recommendations would you make to the pilot regarding long-term oral anticoagulation and/or antiplatelet therapy to prevent ischemic stroke?
 - A. No anticoagulation or antiplatelet medication needed.
 - B. Aspirin 81–325 mg daily.
 - C. Warfarin with an international normalized ratio goal of 2.0 to 3.0.
 - D. Direct oral anticoagulants (e.g., apixaban).

ANSWER/DISCUSSION

2. A. Thromboembolism is a common complication of A-fib, and the American Heart Association recommends a risk-based anticoagulant therapy approach. This can be done with the CHA_2DS_2 -VAS_c score. The risk factors worth 1 point are congestive heart failure, hypertension, diabetes mellitus, vascular disease, age 65–74 yr, and sex (female), and those worth 2 points are age > 75 yr and history of stroke, transient ischemic attack,

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or systemic embolism. People who have a score of 0 have a 0.2% annual risk of ischemic stroke. Risk increases with a higher score, e.g., 2 points is 2.2% risk while 9 points is 12.2%. Oral anticoagulation is currently recommended for a score of 2 or greater in men and 3 or greater in women. Treatment options include nonvitamin K oral anticoagulants like apixaban or more traditional medication like warfarin.⁸ Therapy, however, needs to be balanced with the risk of bleeding, and the HAS-BLED score can be used for this. Since our pilot's CHA₂DS₂-VAS_c score is 0, he is not at a significant risk for thromboembolic stroke due to his A-fib; therefore, anticoagulation therapy is not indicated.

The pilot remained symptom free and was evaluated at the Aeromedical Consult Service for waiver consideration to return to flying duties. He underwent a maximal treadmill stress test that showed rare ventricular ectopy but no other arrhythmia or evidence of ischemia. He had a normal electrocardiogram, 24-h Holter monitor, and echocardiogram. He underwent cardiac monitoring during an F-16 protocol centrifuge ride that showed a normal cardiac response to + G_z , with only three ectopic atrial beats, and no A-fib or other arrhythmias in the +3 G_z to +9 G_z profile.

- 3. What physiological stressors may increase the risk for hemodynamically unstable A-fib?
 - A. Vibration.
 - B. Spatial disorientation.
 - C. +G_z.
 - D. Thermal stress.

ANSWER/DISCUSSION

3. C. A-fib results in a decrease in cardiac output due to loss of the atrial contribution, atrioventricular synchrony, and, if developed, rapid ventricular response.⁵ This may not be enough to be clinically significant at +1 G₂; however, in highperformance aircraft like our pilot's F-16, this could be enough to decrease +G_z tolerance and increase the risk of G-induced loss of consciousness.¹¹ The normal effect of a high $+G_{z}$ environment is a decrease in cardiac output by 20% when subjected to +4 G_z. In a 2004 study of 195 male Japan Air Self-Defense Force fighter pilots, 85.6% had arrhythmias during centrifuge training; 14.4% of these pilots had clinically significant arrhythmias and one pilot had an episode of paroxysmal atrial fibrillation.⁶ Finally, if a pilot requires medications such as beta blockers to control his or her A-fib, the medications could also reduce $+G_{a}$ tolerance to an unacceptable level. The ability of the heart to adequately supply oxygenated blood to the brain is critical when operating in the high $+G_z$ environment; therefore, A-fib has historically been a permanently disqualifying condition in high-performance pilots in all branches of the U.S. military. Traditionally waivers are granted for episodes with a precipitating factor like holiday heart.^{1,10,13} The Federal Aviation Administration requires all cases of A-fib to be deferred, so the airman will require a special issuance.²

Based on the pilot demonstrating no recurrence of A-fib after a 6-mo waiting period, minimal risk factors for recurrence, a normal heart structure, a low risk for thromboembolic event without anticoagulation, and his ability to perform a +9 G_z centrifuge profile without pathological arrhythmias, it was felt that he was at low risk for sudden incapacitation in the F-16. This pilot is the first U.S. Air Force high-performance pilot with paroxysmal A-fib recommended for return to unrestricted flight duties.

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FEBRUARY 1998

North is up...I think (NASA-Ames Research Center, Mountain View, CA; San Jose State U., CA): "Background: If an observer first learns to recognize an object in a specific orientation, a significant increase in processing time usually occurs when the object is subsequently seen in a different orientation; this phenomenon is called the 'misorientation effect.' The present study examines how quickly and how accurately human observers discriminate between airport maps that are viewed in orientations other than those in which they were initially learned. Method: Participants were trained to discriminate between two navigation maps that were seen in only one orientation; they subsequently were tested with maps and aerial photographs of the same airports that were presented in various orientations. Results and Conclusions: There were three principal findings: a) discriminative responses to maps of airports were most rapid when the maps were seen in the same orientation as that in which they were initially learned; b) a significant reduction in reaction time (RT) occurred with repeated presentations of the misoriented stimuli; and c) information learned from navigation maps was not sufficient for all observers to recognize aerial photographs of the same airports."3

FEBRUARY 1973

Prospects of artificial gravity (National Aeronautics and Space Administration, Washington, DC): "This paper reviews findings for American astronauts which may indicate some alteration in vestibular response related to exposure to zero gravity. Of 25 individuals participating in Apollo missions 7-15, nine have experienced symptomatology that could be related to the vestibular system. The apparent divergence between these results and Soviet space program experiences, which initially appears great, may reflect the greater emphasis given by Soviet investigators to vestibular aberrations. Presently the incidence of motion sickness, long known as an indicator of vestibular disturbance, seems too low to warrant any positive statement regarding inclusion of an artificial gravity system in future long-term space missions. Where motion sickness has occurred, adaptation to weightlessness has always resulted in abatement of symptoms. In the absence of biomedical justification for incorporating artificial gravity systems in long-term space flight vehicles, engineering considerations may dictate the manner in which the final ballot is cast."1

Impact of pilot workload (RAF Institute of Aviation Medicine, Farnborough, Hampshire, UK): "The workload of a pilot during the let down of a Boeing 707 was modified by coupling the aircraft to the I.L.S. localiser and glide slope path (coupled approach) or by increasing the participation of the co-pilot in the handling of the aircraft (shared approach). The electrocardiogram of the pilot was recorded during the let down and finger tremor was recorded after landing. The mean rr intervals around touch down of the coupled approaches, which were all of low workload, were increased compared with let downs of equal difficulty handled throughout by the pilot (manual let down). In the shared approaches to 1,000 ft the relation between the mean rr interval around touch down and workload was similar to that for manual let downs but shared approaches to 500 ft increased the mean rr interval around touch down over let downs of a wide range of difficulty. The appearance of finger tremor was not affected directly by the modified workload approaches. It is concluded that flight deck workload patterns during the initial part of the approach influence the neurological state of the pilot around touch down."⁴

FEBRUARY 1948

Man-machine interface (Office of Naval Research, Port Washington, NY): "The importance of considering the human factor in aircraft design and function does not require emphasis and elaboration before this association. As in the case of many other modern technological developments, the physical and engineering sciences have now produced types of aircraft whose over-all performance is, or soon will be, bound by the psychobiological characteristics of their operators rather than by engineering design or structural limitations. Because of this circumstance it became necessary to introduce the concept of designing equipment in terms of its operator. Within the past few years this notion has been expounded by representatives of the various medical sciences, and we find that teams of medical men, physiologists and psychologists are now engaged in joint effort with aeronautical engineers to produce the optical man-machine combination...

"The pilot's relationship to the machine which he directs may be analyzed into three aspects of equipment, namely, *display*, *layout*, and *control*...

"For the avoidance of fatigue in long-duration air operations, the posture of the pilot and other crew members deserves careful consideration...

"The Human Engineering Section of the Special Devices Center of the Office of Naval Research is administering contracts in the field of human engineering...

"One final human engineering project should be mentioned. The psychologist and the engineer have been brought together as a working team only during the past few years. It has become recognized that there is something to be gained by designing equipment in terms of the man who must use it."²

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