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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.

AEROSPACE MEDICAL ASSOCIATION is an organization devoted to charitable, educational, and scientific purposes. The Association was founded when the rapid expansion of aviation made evident the need for physicians with specialized knowledge of the flight environment. Since then, physicians have been joined in this Association by professionals from many fields and from many countries, all linked by a common interest in the health and safety of those who venture into challenging environments.

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

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NOMINATE A COLLEAGUE FOR AN AsMA AWARD!

The deadline is January 15!

The Award Submission Site is open for nominations. Log in to the Members Only section of the AsMA website: www.asma.org. On the left menu you will find a link to the online award nominations system.

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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CLASSIFIED ADS

POSITIONS AVAILABLE

Aerospace Medicine Physicians

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Minimum Qualifications

Possesses a MD or DO degree from an approved school of medicine or osteopathy

Board Certified or Board Eligible. If not board certified, proof of completion of a residency program

Minimum of 3 years of U.S.G. Operations, NASA or Military Flight Surgeon experience

Possess current Basic Life Support (BLS)

Possess a valid, full, active, unrestricted medical license in good standing from any U.S. jurisdiction

Possess current DEA registration.

Ability to complete favorable Credentialing and Security

Must have a minimum of 35 hours of direct patient care in the past year. In addition, the applicant must have a minimum of 3 years in the last 10 years of U.S.G. Operations, NASA or Military Flight Surgeon experience

Argent Technologies, LLC is a Service Disabled Veteran Owned Small Business (SDVOSB), specializing in the provision and management of highly trained professionals in the areas of Medicine, Engineering and Logistics

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For details and to apply, please visit the company website at www.argenttech.net or contact Dr. Romie Richardson: romie@argenttech.net or Pamela Patton: pfp@argenttech.net

NEW ORLEANS, LA

ADVANCE REGISTRATION FORM
AEROSPACE MEDICAL ASSOCIATION
93rd ANNUAL SCIENTIFIC MEETING

MAY 21 – 25, 2023

- **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 STRONGLY ENCOURAGE ONLINE REGISTRATION:

https://www.asma.org/scientific-meetings/asma-annual-scientific-meeting/registration

You **MUST** be an active member of **AsMA** in order to register at the member rate. **Registration fee does not include membership dues.**

Fax registration form with credit card information to: (703) 739-9652

NAME			DEGREE/CREDENTIALS
ORGANIZATION		TITLE	
STREET ADDRESS	CITY	STATE/COUNTRY	ZIPCODE/MAIL CODE
EMAIL	TELEPHONE NUMBER	MOBILE PHONE NUMBER	FAX NUMBER

☐ **Please indicate if this is an address change to your AsMA Membership Record**

First time attendee, or new member? YES ☐ NO ☐ Special dietary requirement: _____

If you are being funded by the U.S. DoD please indicate Branch: ☐Army ☐Navy ☐Air Force ☐Coast Guard

By registering to attend an Aerospace Medical Association (AsMA) conference, you grant permission to AsMA to take and use your photo in AsMA marketing and promotional pieces for an indefinite period of time. Marketing and promotional pieces include, but are not limited to, printed brochures, reports, postcards, flyers, and materials, as well as online uses such as postings on the AsMA website, online newsletters, and e-mail blasts. AsMA shall own all rights, including copyrights in and to the photos.

You also grant permission to AsMA to use, encode, digitize, transmit, and display the video/audio of your session, presentation, or workshop given at the AsMA conference, singularly or in conjunction with other recordings, as well as to use your name, photograph, biographic information, and ancillary material in connection with such video/audio for commercial, promotional, advertising, and other business purposes. AsMA and its employees are released from any liability arising out of the use of your name, video, photographs, and/or organization name and location.

REGISTRATION FEE	EARLY BIRD† 1/1 – 1/31	ADVANCE 2/1 – 5/12	AT-THE-DOOR 5/21 – 5/25	REGISTRATION FEE REMITTED
☐MEMBER	$450†	$550	$650	
☐NON-MEMBER	$725†*	$850*	$950*	
☐NON-MEMBER PRESENTER	$625†*	$750*	$850*	
☐RESIDENTS	$325†	$400	$400	
☐STUDENTS	$75†	$125	$125	
☐FAA-AME SEMINAR§	$325†	$400	$400	
			REGISTRATION FEE SUBTOTAL ➔	

***Go to www.asma.org to become a member and take advantage of the reduced registration rates, receive the official Aerospace Medical Association journal, and other membership benefits.**

†***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.

(See reverse for workshops & events)

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

WORKSHOP DATE/NAME		FEE	Total Fee
☐ Sun., May 21, 8:00 am – 11:30 am Workshop: "Aerospace Medicine Faculty Development" (MAX 75)		$85	
☐ Sun., May 21, 8:00 am – 4:30 pm Workshop: "Altitude Decompression Sickness – Pathophysiology, Diagnosis, Treatment, and Mitigation" (MAX 75)		$175	
☐ Sun., May 21, 9:00 am – 4:30 pm Workshop: "Establishing Peer Support Programs Across All Aviation Sectors" (MAX 75)		$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 a.m., Richard B. "Dick" Trumbo 5K Fun Run/Walk ***(Advance Purchase Only)***		$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 ***(Advance Purchase Only)***		$50	
☐ Mon. May 22, Fellows Dinner ***(Advance Purchase Only)*** **(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, 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.

REGISTRANTS SUBMITTING VIA FAX MUST INCLUDE CREDIT CARD INFORMATION.

PAYMENT METHOD: **Check Number:** _____ ☐ **CHECK** ☐ **AMEX** ☐ **DISCOVER** ☐ **MASTERCARD** ☐ **VISA** ☐ **DINERS**

Name as it appears on card: (**PLEASE PRINT**)_____

Credit Card #_____Exp. Date: _____ Security Code: _____

Street: _____ City: _____ State: _____ Zip/Mail Code: _____

Signature _____Country: _____

Fax with credit card information to:
(703) 739-9652
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Mail with payment to:
Aerospace Medical Association
320 S Henry Street
Alexandria, VA 22314-3579

FAX TO (703) 739-9652. PLEASE REMEMBER TO INCLUDE BOTH SIDES WHEN FAXING.
*****USE ONLY ONE METHOD TO REGISTER*****

May 21 - 25, 2023
Sheraton New Orleans
New Orleans, Louisiana

The WING of AsMA
AsMA 93rd Annual Scientific Meeting

REGISTRATION FORM

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.**

NOTE: Registration is mandatory for participation in Wing activities.
Register before May 1, 2023 to save $5 each on dues & registration. After that date, dues & registration will be $40 each.

Wing Dues (May 2023 – May 2024) _____New Member 2023 _____Renewal _____2023 Dues Previously Paid	$35.00 /$40.00	$_____
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.____ $ 0.00
Tuesday, May 23, 8:30 AM – 12:00 PM (Meet in Lobby @ 8:15 AM) Swamp Adventure – High Speed Airboat Tour* *SEE IMPORTANT DISCLOSURES	$75.00	No.____ $_____
OR		
Tuesday, May 23, 8:30 AM – 12:00 PM (Meet in Lobby @ 8:15 AM) Swamp Adventure - Swamp Boat Tour	$55.00	No.____ $_____
OR		
Tuesday, May 23, 9:30 AM – 2:00 PM (Meet in Lobby @ 9:30 AM) Self-Guided St. Charles Streetcar Tour Pay as you go …		No.____
Wednesday, May 24, 10:00 AM – 1:00 PM (Meet in Lobby @ 9:30 AM) Annual Wing Buncheon & 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) Mardi Gras Museum & Mask Making Class	$65.00	No.____ $_____
	TOTAL	**$**_____

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
OR
Mail this form and your check (payable to Wing of AsMA in US DOLLARS) to:
Brenda Clinton, Treasurer 10603 Derby Mesa Ct – Colorado Springs, CO 80924

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. *Remember to bring a small gift reminiscent of your home city, state or country for the gift exchange and please include a short note letting the recipient know who/where the gift is from.* ***New members and first-time attendees don't bring a gift as we are very happy to welcome you to THE WING!***

This year's Welcome Reception will be held in **THE SHERATON NEW ORLEANS HOTEL** ***"Grand Couteau" Room.***

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

Tuesday, May 23, 8:30 AM – 12:00 PM $75.00

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. ***BECAUSE OF THE NATURE OF THE AIRBOAT RIDE, PREGNANT WOMEN OR PEOPLE WITH NECK OR BACK PROBLEMS CANNOT PARTICIPATE. HEARING PROTECTION IS PROVIDED BY THE COMPANY. YOU CAN PURCHASE INEXPENSIVE RAIN PONCHOS AT THE SWAMP TOUR SNACK SHOP.***

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

Tuesday, May 23, 8:30 AM – 12:00 PM $ 55.00

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 $ Pay as you go

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 ***you*** design as you go.

ANNUAL WING BRUNCHEON & BUSINESS MEETING
NEW ORLEANS SCHOOL OF COOKING **$ 50.00**
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 **$ 65.00**
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

NOMINATE YOUR COLLEAGUE FOR AN AEROSPACE MEDICAL ASSOCIATION ANNUAL AWARD!

THE DEADLINE IS JANUARY 15!

The Award Submisison Site is open for nominations!

Log in to the Members Only section of the AsMA website: ***www.asma.org***
On the left menu you will find a link to the online award nominations system.

Farewell and Welcome!

Frederick Bonato, Ph.D., FAsMA

This editorial is entirely devoted to transitions on the Journal team. It is difficult to write. Since 2010 when I first took on the role of editor-in-chief I have worked closely with several individuals. I think our work has been worthwhile and effective—and the time certainly did go fast! The amount of work that goes into producing a high-quality monthly scientific journal is profound—but well worth it. Having a well-integrated and collaborative team is critical to success and I have been fortunate to work with a talented and dedicated group. As you read this issue, some transitions at the journal office have already taken place.

I'll start with Pam Day. Some of you may have heard of Pam? I am sure you are aware that Pam has been a mainstay at the Journal and AsMA since 1980. Pam has been a go-to person for many of us, but especially for me in her role as the Journal's Managing Editor. Her dedication to the Journal and the Association is unapparelled. Over the last 13 years I have come to rely on Pam as a trusted partner in maintaining the highest quality journal possible. On a personal note, Pam has become a dear and trusted friend. I expect we will still see Pam in the future—she is a permanent member of the AsMA family.

Fortunately for us, the new Managing Editor is no stranger to the Journal or Association. Rachel Trigg, Assistant Managing Editor, will take on the responsibility of the Managing Editor role. Rachel has been with the journal nearly 20 years and started as an editorial assistant in 2003. She has a wealth of experience that will serve her well in her new role as Managing Editor. I have always worked well with Rachel and know that will continue moving forward.

Early on in my tenure as editor-in-chief, Deb Sventek became the Assistant to the Editor. Deb has been my right hand in many ways and we have worked together on approximately 3000 journal submissions over the last 10 years. It has been a pleasure to work with Deb over the years and I appreciate all that she has done. I am pleased that Sandy Kawano is coming on board as the new Assistant to the Editor. I had a chance to meet and speak with Sandy during the AsMA meeting in Reno and feel she is the right person for this important role. Deb will work with Sandy through the end of 2022 to provide her training for the position.

Finally, Dr. Michael Barratt has decided to step down as the Associate Editor for Space Medicine. Mike has been a go to person for me on many issues over the last 13 years. His knowledge, experience, and network have been important for our success in the area of space medicine. Despite his busy 'day job' as a NASA astronaut, Mike has always been available to help make the journal better. Currently, a new Associate Editor is being sought and we hope to have one in place very soon.

As I start my last year as Editor-in-Chief of the Journal, I am grateful for all the contributions of Pam Day, Deb Sventek, and Mike Barratt. It will be different kind of year without them. That said, I am looking forward to working with Rachel Trigg and Sandy Kawano as they start their roles. I wish to also thank all our volunteer referees who contribute to the success of the Blue Journal throughout the year! The Journal would not be possible without your efforts. Thanks also to the Editorial Board who I rely on throughout the year. I encourage you to submit your work to AMHP or serving as a reviewer. Please do not hesitate to contact us with any questions or comments you may have at: AMHPjournal@asma.org.

Wishing you a happy and productive 2023!

DOI: https://doi.org/10.3357/AMHP.941Editorial.2023

Prepping for New Orleans

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

As you read this, it is January 2023, but as I write this, it is still November and we just finished the November Council meeting and the Scientific Program abstract review process. It has been a busy autumn! The business of AsMA never stops.

First, let me thank the people who submitted abstracts. We had over 500 to review. Pam Day and the Scientific Program Committee had about a week to get all the abstracts grouped according to topic area. The actual review process was completed both virtually in early November and in person November 17, 2022. Each abstract was evaluated by three virtual reviewers and then in person by a team. The final scientific, panel, and poster sessions look exciting and informative. If you see the following individuals, thank them for their hard work! In addition, we are always looking for volunteers in this very important work.

- Ian Mollan, Scientific Program Committee Chair
- Ellis Boudreau, Deputy Chair
- Adam Sirek and Jaime Harvey, Remote Review Coordinators
- Douglas Boyd, Panels Chair
- Amanda Lippert, Slide Chair
- Samir Alvi, Posters Chair
- Katie Samoil, Member at Large
- Chuck Reese, Immediate Past Chair

Did you know there is a mentoring program for new authors for both submitting abstracts and preparing the actual presentation? If you are new to this process or want to brush up your skills, don't hesitate to reach out to Barry Shender and he and his team will help.

Another significant event during Council was appointing an Ad Hoc Committee on Commercial Spaceflight. The team is working to develop a repository of existing articles and studies on Commercial Spaceflight for passenger/participant health. As the flights become more frequent and affordable, your association is working to keep science in the decision process. Literally, the heavens are the limit of what we can do.

Finally, let me wish you a productive and safe New Year.

DOI: https://doi.org/10.3357/AMHP.941PP.2023

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

Cabin Pressure Altitude Effect on Acceleration Atelectasis After Agile Flight Breathing 60% Oxygen

Henry Tank; Gareth Kennedy; Ross Pollock; Peter Hodkinson; Rebecca-Anne Sheppard-Hickey; Jeffrey Woolford; Nicholas D. C. Green; Alec Stevenson

INTRODUCTION: A flight trial was conducted to determine whether breathing 60% oxygen during high performance flight maneuvers using contemporary pilot flight equipment induces atelectasis and to explore whether cabin altitude had any influence on the extent of atelectasis identified.

METHODS: On 2 separate days, 14 male aircrew flew as passengers at High [14,500–18,000 ft (4420–5486 m)] and Low [4000–6000 ft (1219–1829 m)] cabin pressure altitude in a Hawk T Mk1 aircraft breathing 60% oxygen. Sorties comprised 16 maneuvers at +5 G_z, each sustained for 30 s. Lung volumes (spirometry), basal lung volume (electrical impedance tomography, EIT), and peripheral oxygen saturation during transition from hyperoxia to hypoxia (pulmonary shunt fraction) were measured in the cockpit immediately before (Pre) and after (Post) flight.

RESULTS: Forced inspiratory vital capacity (FIVC) was significantly lower Postflight after High (−0.24 L) and Low (−0.38 L) sorties, but recovered to Preflight values by the fourth repeat (FIVC4). EIT-derived measures of FIVC decreased after High (−3.3%) and Low (−4.4%) sorties but did not recover to baseline by FIVC4. FIVC reductions were attributable to decreased inspiratory capacity. S_pO_2 was lower Postflight than Preflight in High and Low sorties.

DISCUSSION: Breathing 60% oxygen during flight results in a 3.8–4.9% reduction in lung volume associated with a small decrease in blood oxygenation and an estimated pulmonary shunt of up to 5.7%. EIT measures suggest persisting airway closure despite repeated FIVC maneuvers. There was no meaningful influence of cabin pressure altitude. The operational consequence of the observed changes is likely to be small.

KEYWORDS: atelectasis, forced inspiratory vital capacity, acceleration, altitude.

Tank H, Kennedy G, Pollock R, Hodkinson P, Sheppard-Hickey R-A, Woolford J, Green NDC, Stevenson A. *Cabin pressure altitude effect on acceleration atelectasis after agile flight breathing 60% oxygen*. Aerosp Med Hum Perform. 2023; 94(1):3–10.

Pulmonary acceleration atelectasis may account for some currently unexplained symptomatic in-flight physiological events.[7] In the United Kingdom, aircrew questionnaires have suggested that acceleration atelectasis has occurred during sorties in the Hawk T2 fast jet trainer.[20] The main factors associated with the development of acceleration atelectasis are sustained head-to-foot (+G_z) acceleration, anti-G trouser inflation, and high inspired oxygen concentrations (hyperoxia).[8,17] Common manifestations include postflight urge to cough, paroxysmal coughing, shortness of breath, chest tightness, and substernal discomfort on inspiration.[4,8,25] This is associated with marked attenuation of postflight vital capacity (VC)[16,17,25] by up to 60%.[24] The attenuation in VC is often reversed by deep breaths and, to provide a surrogate for the degree of atelectasis present, an inspiratory measure, rather than the more usual expiratory measure of VC, is typically used. This minimizes any atelectasis clearance prior to the VC measure. Forced inspiratory vital capacity (FIVC) is usually seen to revert to normal with repetition of the maneuver or following coughing or deep breathing. Research on the centrifuge has also demonstrated that a

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significant pulmonary shunt can develop,[10] a phenomenon known to be associated with atelectasis.[14]

The mechanism underlying development of acceleration atelectasis is understood to be absorption of gas trapped in the alveolar space when distal airways become occluded.[13,18,24] Exposure to $+G_z$ exaggerates intrapleural pressure gradients,[8] while anti-G trouser inflation splints the diaphragm and limits caudal expansion of the lung bases.[13] If alveolar gas contains a high concentration of oxygen that is rapidly absorbed once the airways close, the residual gas pressure can become inadequate to prevent alveolar collapse. It is generally accepted that retaining at least 40% inert gas (i.e., nitrogen) in the breathing supply, equivalent in practice to limiting the fractional inspired oxygen concentration (F_IO_2) to a maximum of 60%, prevents the development of meaningful atelectasis.[6] Previous research[15] exposing centrifuge subjects to a 4.5-min simulated air combat maneuver (SACM) consisting of +4.5 G_z peaks interspersed with +3 G_z nadirs monitored FIVC pre- and post-centrifuge undertaken with F_IO_2 varying from 21–100%. Postexposure FIVC, reported as a percentage of pre-exposure values, was decreased by 11%, 18%, 24%, and 26% with an F_IO_2 of 70%, 82.5%, 95%, and 100%, respectively, while no reduction was seen with an F_IO_2 of 50%. Based on a linear regression between F_IO_2 and the reductions in FIVC reported, a 5% fall in FIVC might be expected with an F_IO_2 of 60%.

There is a limited range of possible reasons why acceleration atelectasis reported in flight might result in a greater decrease in FIVC. The F_IO_2 could be higher than expected or, alternatively, the G profiles being flown may be more conducive to atelectasis formation in some aircraft types. Alternatively, evolving aircraft capabilities and newer designs of anti-G protection systems might predispose to the development of acceleration atelectasis, such as the use of full coverage anti-G trousers (FCAGT) with more efficient abdominal compression and splinting of the diaphragm. The improved G protection afforded by these garments[22] also means that pilots can sustain high levels of $+G_z$ acceleration for longer, potentially without recourse to the anti-G straining maneuver (AGSM), which is known to be effective at inhibiting atelectasis formation.[24]

It is possible that other features of the flight environment may affect atelectasis, such as the reduced ambient pressure.[3] Ernsting[5] reported the kinetics of trapped gas absorption in the dog lung, which followed a two-phased profile. Initially, absorption of oxygen from alveoli distal to closed airways was rapid, determined principally by gas solubility (independent of the presence of nitrogen); thereafter, the rate of absorption was proportional to regional blood flow and became slower with higher nitrogen concentrations. At altitude, the rate of the first phase was more rapid, while the second phase was slower. Ernsting concluded that the overall effect of altitude was to slow the rate of alveolar collapse and thereby impede atelectasis formation.

The aims of the current study were to determine whether breathing 60% oxygen (balance 40% nitrogen) during high performance flight maneuvers induces atelectasis and to explore whether cabin altitude had any influence on the extent of atelectasis identified. Measures were taken before and after (but not during) flight. The presence (and extent) of atelectasis was inferred from changes in FIVC and indices derived from electrical impedance tomography (EIT), which provides a surrogate measure of regional (basal) lung volume. Blood oxygen saturation and a derived estimate of pulmonary shunt were also recorded. The null hypotheses were that breathing 60% oxygen would prevent atelectasis development and there would be no influence of cabin altitude.

METHODS

Subjects

Recruited were 14 healthy male aircrew. All aircrew held a current flight medical and had previous fighter aircraft experience on platforms such as Alpha Jet, Hawk, Talon, Tornado, Tutor, and Typhoon. The study protocol was approved by the UK Ministry of Defense Research Ethics Committee and adhered to the principles outlined in the Declaration of Helsinki. Informed written consent was provided by all participants.

Equipment

Flights were conducted in a modified Hawk T Mk1 aircraft flying from Boscombe Down, Wiltshire, United Kingdom. For this trial the participant sat in the rear seat while the front seat was occupied by a safety pilot who handled the aircraft during maneuvers. Typhoon aircrew equipment assemblies (AEA) were worn by both the participant and safety pilot, and included a flying coverall, FCAGT, flight jacket (incorporating chest counterpressure; CCP), aircrew boots, an Mk 10 helmet, and P/Q oxygen mask. FCAGT pressurization, pressure breathing for G protection (PBG), and CCP inflation were provided from a Typhoon breathing and anti-G regulator (aircrew services package; ASP). FCAGT pressurization commenced at +2 G_z (±0.3 G), increasing by 10 kPa · G^{-1}. PBG began at +4 G_z, increasing at 1.6 kPa · G^{-1} with the CCP inflated to an equivalent pressure (±1.3 kPa). All AEA was fitted by a qualified Survival Equipment Technician on the first day of testing and proper fit was verified prior to each trial flight.

Protocol

Each participant underwent two flights on separate days. The flight sorties were, in so far as practicable, identical, only differing in the cabin altitude (ALT) to which the participant and safety pilot were exposed. The low altitude sortie (Low) was flown at flight altitudes where the target cabin altitude remained between 4000–6000 ft (1219–1829 m) pressure altitude (PA) (609–656 mmHg). The high-altitude sortie (High) was flown at flight altitudes where the target cabin altitude remained between 15,000–18,000 ft PA (4420–5486 m; 380–429 mmHg). The upper limit of 18,000 ft PA was selected to minimize risk of decompression sickness and the range represents the highest likely cabin altitudes during dynamic maneuvering in a high-performance fighter. Due to aircraft performance limitations with the Hawk T Mk1, the high-altitude sortie (High) was

undertaken with the cockpit depressurized so that a higher cabin altitude could be achieved. This allowed the G profiles to be flown at a lower flight altitude than would otherwise be necessary to achieve the required 18,000-ft PA cabin altitude [the cabin altitude remained 1000–2000 ft (305–610 m) lower than the aircraft altitude due to the effects of aircraft speed on cabin ram air flow]. To achieve and sustain the acceleration profiles for the High sorties, the safety pilot had to perform the turn in a descending spiral, starting at a flight altitude of around 20,000 ft PA (6096 m; 349 mmHg). Aircraft altitude for maneuvers in the Low sorties where the cabin was pressurized were around 6000 ft (609 mmHg). Cabin pressure data were not recorded in flight due to limitations with instrumentation, but cabin altitude was confirmed using aircraft instrumentation and recorded manually on the crew's kneeboard.

Performance limitations of the Hawk T1 placed greater constraints on the High sortie and risked limiting the number of G exposures that could be completed. Accordingly, the High sorties were flown first by all participants so that their total $+G_z$ exposure could always be replicated accurately during their subsequent Low sortie. Matching $+G_z$ exposures between sorties was prioritized over the possibility of introducing an order effect.

Preflight measurements were undertaken immediately prior to donning a flight helmet and again 15 min before takeoff. Soon after takeoff, a series of G exposures were performed as a subject 'warm-up' and to confirm operability of the anti-G system. This comprised a rapid onset rate turn to +4 G_z for 15 s followed by +6 G_z for the same duration. The trial maneuvers began 10–15 min after takeoff and within 30 min of preflight measurements. Trial maneuvers consisted of 16 repeats at +5 G_z maintained at this acceleration level for approximately 30 s, each attained using rapid acceleration onset rates (>6 $G \cdot s^{-1}$). The G profiles were separated by approximately 90 s of level flight. In addition, participants were instructed to avoid using the AGSM during the test G profiles if possible and apply lower body muscle tensing only to augment their G protection as required. Throughout all flights, participants breathed a 60% oxygen (balance nitrogen) gas mix, supplied from a series of compressed gas cylinders via the Typhoon ASP. After landing, the aircraft taxied to the apron, powered down, and was towed into the hangar where the measurements made pre-exposure were repeated. The time between landing and the performance of the postflight measurements was ~15 min and from the last $+G_z$ maneuver around 30 min.

Pre- and Postflight Measurements

Before (Pre) and after each flight (Post) a series of measurements were made in the aircraft hangar. For these measures the aircrew were fully clothed in their AEA and remained seated and harnessed in the ejection seat of the aircraft. Tests were undertaken using a standard respiratory mask (Hans Rudolph Inc., Shawnee, KS, USA) to which a pneumotachograph (Fleisch type, No. 2) and differential pressure transducer (Celesco low cost variable reluctance, 0–2 cm H_2O; Celesco Transducer Products, Inc., Chatsworth, CA, USA) had been fitted. Inspiratory and expiratory valves were housed in a machined plastic t-piece fitted upstream of the pneumotachograph. The mask inspiratory hose was connected to a set of manual valves which selected the breathing gas: either air, 100% oxygen, or a 14% oxygen (balance nitrogen) gas mix. The latter two were bottled gases supplied to the participant via an independent pressure demand regulator. The flowmeter was calibrated across a range of flows before testing began and immediately after the measurements had been performed using a calibration syringe. Following Pre measurements, participants immediately donned their oronasal P/Q oxygen mask and flight helmet and start-up procedures were commenced. Upon return to the hangar postexposure, participants again donned the test mask as soon as their oronasal P/Q oxygen mask and flight helmet had been removed.

While breathing air through the test mask, the participant was instructed to expire to their normal end-expiratory position and to indicate when this was reached. An experimenter then selected 100% oxygen, which the participant breathed until the expired nitrogen concentration fell below 1%. The participant was then supplied with the hypoxic gas mix (14% oxygen, balance nitrogen); when a stable end-tidal oxygen concentration was achieved, they completed four FIVC maneuvers (i.e., FIVC1, FIVC2, etc.) separated by periods of tidal breathing (around 45 s). Each FIVC comprised forceful emptying of the lungs followed by a maximal inspiration in accordance with current guidelines.[9]

Inspired and expired partial pressures of nitrogen, oxygen, carbon dioxide, and argon were initially measured using a respiratory mass spectrometer (MSX-671, Ferraris-Respiratory Europe Ltd., Hertfordshire, UK). However, a technical fault meant that in eight subjects, measurements of partial pressures of oxygen and carbon dioxide were made using a laser gas analyzer (O_2Cap, Oxigraf Inc., Sunnyvale, CA, USA). Peripheral arterial oxygen saturation (S_pO_2) was determined using a pulse oximeter (Model 3900, Datex-Ohmeda, Madison, WI, USA) fitted to the ear lobe. Ambient temperature, pressure, and humidity were recorded daily (WMR86A Backyard Pro Wireless Weather Station, Oregon Scientific, High Wycombe, UK). A further temperature measurement was made within the mask housing using a thermocouple (T-type, AD Instruments, Dunedin, New Zealand). All data were recorded using an analog-to-digital converter and PC-based acquisition system (PowerLab 16/30, AD Instruments, Dunedin, New Zealand).

In addition, changes in a surrogate measure of regional lung volume were investigated using EIT. This technique exploits the principle that with increasing air volume the lung parenchyma present greater resistance to the flow of an electrical current. By applying an imperceptible alternating current between successive pairs of electrodes and measuring the resultant voltage distribution circumferentially around the chest, cross-sectional imagery of thoracic impedance can be generated. At high temporal resolution changes in impedance with the breathing cycle can be visualized and quantified, for the whole section or a region of interest, and may be particularly sensitive to changes affecting basal lung regions. For this study

a Pulmovista®500 device (Dräger, Lübeck, Germany) was used with a 16-electrode belt fitted at the fifth intercostal space. Adhesive electrode gel (Tensive, Parker Labs, Fairfield, NJ, USA) was applied to the dry electrodes to improve skin contact and reduce movement of the belt; a form fit foam pad was used to ensure the electrodes across the back retained good contact with the skin, especially along the anatomical indentation formed by the thoracic spinous processes.

Data Analysis

Inspired and expired volumes were derived by integration of the inspired and expired flow, respectively. Tidal volume (V_T) and FIVC were identified using a cyclic peak/nadir detection algorithm available in the data analysis software. Respiratory rate (RR) and V_T were averaged over a 2-min period 30 s prior to commencement of the first FIVC while breathing the hypoxic (14% O_2) gas mix. Inspiratory capacity (IC) and expiratory reserve volume (ERV) were computed as the difference in the mean end-tidal volume from 3–5 tidal breaths prior to each FIVC and the minimum and maximum volumes during the expiratory and inspiratory phases of the FIVC, respectively. Reported volumes are all corrected to Body Temperature and Pressure, Saturated conditions (BTPS). For measurements made by EIT, equivalent impedance measures of FIVC ($FIVC_{EIT}$) were derived. All impedance changes were referenced to the minimum impedance recorded during the FIVC maneuvers and, therefore, represent increases from residual volume. The reported end-tidal partial pressures of oxygen ($P_{ET}O_2$) and carbon dioxide ($P_{ET}CO_2$) are those recorded during the expiratory phase of the FIVC maneuver, presented as the average across all four repeats. Mean S_pO_2 were extracted over a 2-min period while breathing air immediately after donning the test mask ($S_pO_{2\ normoxia}$), during the final period breathing 100% oxygen ($S_pO_{2\ hyperoxia}$), and 30 s before commencing the first FIVC maneuver while breathing the hypoxic gas mix ($S_pO_{2\ hypoxia}$). Pulmonary shunt (to the nearest percent) was estimated using techniques described elsewhere;[19] briefly, the relationship between the expired fractional end-tidal oxygen concentration ($F_{ET}O_2$) and S_pO_2 during the transition from hyperoxia to hypoxia was compared with standard curves generated from an established model of gas exchange with varying shunt fractions.[21]

Statistical Analysis

The principal comparative measure used to determine sample size was the measurement of FIVC. This is the only metric where previous data of the effect of atelectasis are available. We considered an effect size of greater than a Cohen's *d* of 1 as an important effect (i.e., the difference in FIVC with atelectasis should be larger than the between subject variation in FIVC normally observed). FIVC is approximately 5 L in adults with a standard deviation of 0.6 L. Given that field measurements of FIVC are likely to demonstrate a greater variability than those performed in the laboratory, based on a power of 80%, alpha of 0.05, a correlation between repeated measurements of 0.70 (determined from previous measurements of FIVC using the nitrogen washout technique by one of the experimenters), and an SD of 0.75 L to detect a meaningful pre-post flight difference (i.e., Cohen's $d = 1$), 10 participants were required. In order to account for participant dropout, 14 participants were recruited. Datasets were assessed for a normal distribution using the Shapiro-Wilks test. First, to guide subsequent analysis, the baseline (Pre) FIVC data (FIVC#) before the two sorties (Day) were compared using repeated measures analysis of variance (rmANOVA), interrogating main effects of Day vs. FIVC# vs. Subject. Subsequently, the differences between corresponding FIVC measurements (delta Pre-Post) across the two altitude (ALT) conditions were evaluated using rmANOVA for main effects of ALT vs. Subject vs. FIVC#. Specific post hoc pairwise comparisons to explore changes in FIVC# were conducted using paired *t*-tests. The outcomes of FIVC analyses guided parallel analyses of IC and ERV. EIT measures were analyzed within each ALT condition, as it was not possible to precisely replicate electrode placement between the two flights. EIT data were analyzed for main effects of Subject vs. FIVC#. Data for V_T, RR, and S_pO_2 were subject to rmANOVA to assess main effects of $+G_z$ (Pre/Post) vs. ALT (High/Low) vs. Subject. Specific post hoc comparisons employed paired *t*-tests and Wilcoxon signed rank tests for nonparametric data. For data presentation mean and 95% confidence interval after correction for between subject variability[1] are shown. IBM SPSS Statistics v.22 (Chicago, IL, USA) was used for the statistical analyses with significance for main effects of rmANOVA set at $P < 0.05$.

RESULTS

Demographic information on the 14 male study participants is shown in **Table I**. Cabin altitude at the start of maneuvering in the High condition was 18,000 ± 50 ft (5486 ± 1.5 m) PA and mean finishing altitude was 14,430 ± 1265 ft (4398 ± 386 m) PA. In the Low condition, the cabin altitude achieved was 4300 ± 800 ft (1311 ± 244 m) PA. The mean G_z level reached across the acceleration exposures successfully registered by the flight

Table I. Demographic Data of 14 Male Participants.

SUBJECT	AGE (yr)	HEIGHT (cm)	WEIGHT (kg)	TOTAL FLYING HOURS (h)
1	48	175	75	1471
2	34	178	89	2000
3	50	173	85	6500
4	55	176	88	3850
5	44	171	66	3200
6	37	182	65	2050
7	46	173	68	4365
8	23	174	80	180
9	23	182	77	450
10	41	193	80	3000
11	28	173	65	210
12	40	190	90	3000
13	35	180	81	2800
14	38	173	80	3500
Mean	39	178	78	2613
SD	10	6	9	1891

Table II. Absolute and Differential (Δ) Data for Repeated Measures Taken Pre- and Postflight at High and Low Altitude.

		High			Low		
		Pre	Post		Pre	Post	
VARIABLE		CTRL	$FIVC_1$	$FIVC_4$	CTRL	$FIVC_1$	$FIVC_4$
FIVC	Absolute	4.87 ± 0.18	4.64 ± 0.33*	4.80 ± 0.27	5.08 ± 0.21	4.70 ± 0.25*	4.97 ± 0.31
(L BTPS)	Δ CTRL	–	−0.24 ± 0.18*	−0.07 ± 0.36	–	−0.38 ± 0.37*	−0.10 ± 0.35
IC	Absolute	3.57 ± 0.25	3.35 ± 0.20*	3.62 ± 0.28	3.81 ± 0.20	3.37 ± 0.34*	3.67 ± 1.16
(L BTPS)	Δ CTRL	–	−0.22 ± 0.31*	0.05 ± 0.31	–	−0.44 ± 0.4*	−0.14 ± 0.34
ERV	Absolute	1.34 ± 0.14	1.37 ± 0.14	1.33 ±0.31	1.32 ± 0.17	1.38 ± 0.25	1.35 ± 0.30
(L BTPS)	Δ CTRL	–	0.03 ± 0.19	−0.01 ± 0.33	–	0.06 ± 0.32	0.02 ± 0.29
$FIVC_{EIT}$	Absolute	21.1 ± 7.5	17.8 ± 7.9*	19.2 ± 7.7*	27.7 ± 11.4	23.3 ± 13.1*	25.2 ± 12.8*
(Impedance %)	Δ CTRL	–	−3.3 ± 2.6*	−1.9 ± 2.6*	–	−4.4 ± 4.1*	−2.4 ± 3.3*

CTRL data are the means of four baseline Preflight FIVCs; Δ CTRL represent changes from this mean during Postflight FIVC 1 and FIVC 4. Data (N = 14) are mean ± the 95% confidence interval after correction for between-subject variability.
*Denotes statistical significance on post hoc paired t-tests ($P \leq 0.05$).

recorder (N = 175) was +4.8 ± 0.1 G_z. The mean duration of the $+G_z$ exposures was 33 ± 6 s. Mean G levels (Z = 1.96, P = 0.14) were not significantly different between the High and Low conditions; G durations were longer in the High than Low conditions (Z = 1.96, P < 0.001) by a short interval (35 vs. 32 s).

Lung volume and EIT data are summarized in **Table II**. For ease of comparison, group FIVC data are also shown in **Fig. 1**, including all four repeats performed before (Pre) and after (Post) each flight for both the High and Low cabin altitude conditions. The graph indicates that FIVC was decreased postflight on both days, but that measures tended generally to be higher, including preflight baseline data, on the day of the lower cabin altitude sortie. The rmANOVA examining baseline (Pre) FIVC data for the 2 d confirmed a significant difference between baseline FIVC values for the High and Low cabin altitude conditions (5.1 ± 0.65 vs. 4.9 ± 0.64, P = 0.036). Thus, rmANOVA to assess the influence of cabin altitude on FIVC was conducted using the differential values for corresponding pre- and postflight FIVCs, indicating a main effect of FIVC# (P = 0.048), but no effect of cabin altitude (P = 0.25). Post hoc paired comparisons highlighted that the first FIVC performed following the sortie was lower than mean baseline FIVC for both the High (P = 0.039) and Low cabin altitude conditions (P = 0.002), confirming an effect of flight to decrease FIVC. This recovered fully by FIVC4 such that, for both High and Low cabin altitudes, lung volume at FIVC4 was not significantly different from baseline (Table II). The changes in FIVC were due to a fall in IC, which was decreased from baseline on FIVC1 in both the High (P = 0.02) and Low (P = 0.002) cabin altitude conditions, but had recovered by FIVC4. In contrast, ERV was unaffected (see Table II). Changes in $FIVC_{EIT}$ were similar, with a decrease from baseline seen postflight for both the High (P = 0.003) and

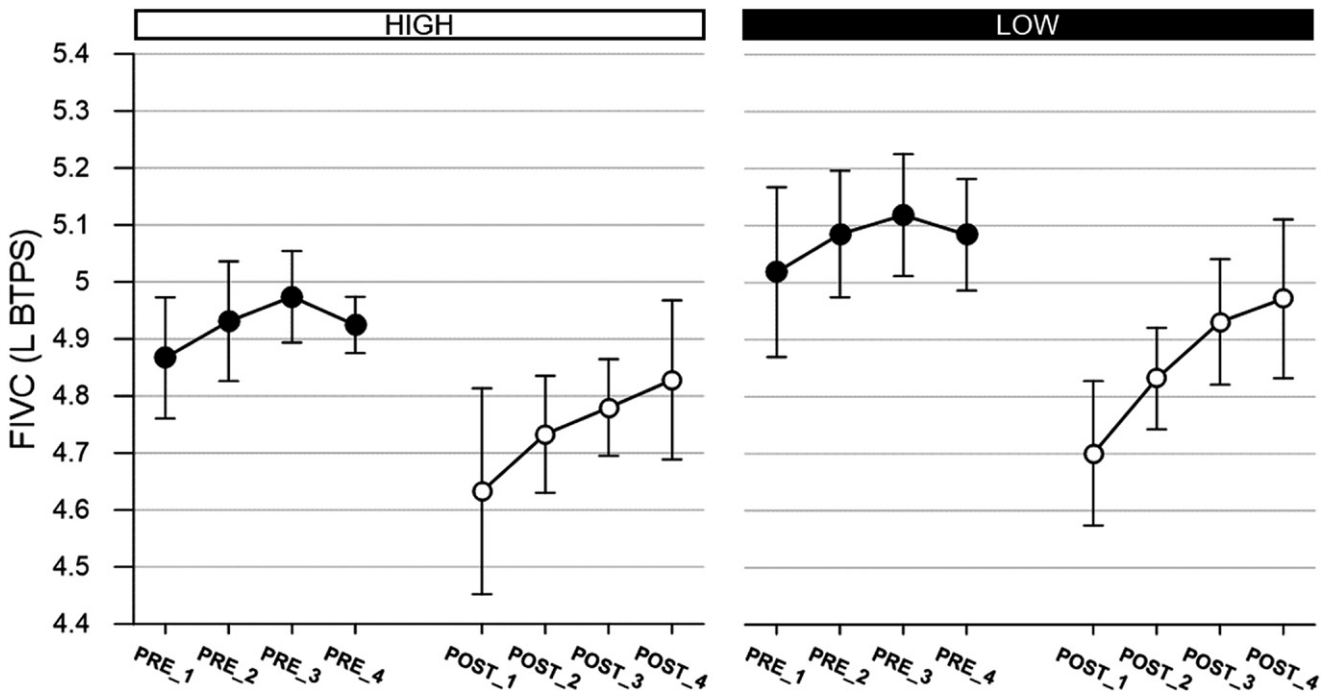

Fig. 1. Forced inspiratory vital capacity measured four times before (Pre; black circles) and after (Post; white circles) the High (left) and Low (right) cabin altitude sortie. Data (N = 14) are mean ± the 95% confidence interval after correction for between-subject variability.

Table III. Data for: S_pO_2 Measurements Whilst Breathing Air, Hyperoxic Gas (100% O_2), and Hypoxic Gas (14% O_2); Tidal Volume ($L \cdot s^{-1}$) and Respiratory Rate (Breaths per Minute) During Pre-FIVC Hypoxia; and End-Tidal Partial Pressures of O_2 ($P_{ET}O_2$) and CO_2 ($P_{ET}CO_2$) during FIVC.

	Pre	Post
$S_pO_{2\ normoxia}$ (%)		
High	97.7 ± 0.6	96.2 ± 0.8*
Low	97.6 ± 0.7	96.5 ± 0.7*
$S_pO_{2\ hyperoxia}$ (%)		
High	99.1 ± 0.6	98.7 ± 0.6*
Low	99.3 ± 0.8	98.6 ± 0.5*
$S_pO_{2\ hypoxia}$ (%)		
High	94.1 ± 0.9	92.3 ± 0.8*
Low	94.5 ± 1.0	92.7 ± 0.9*
Tidal Volume ($L \cdot s^{-1}$)		
High	1.21 ± 0.30	1.11 ± 0.15
Low	1.02 ± 0.16	1.03 ± 0.13
RR (bpm)		
High	11.9 ± 1.2	12.1 ± 1.1
Low	13.7 ± 1.4	13.6 ± 1.3
$P_{ET}O_{2\ hypoxia}$ (mmHg)		
High	68.4 ± 3.8	68.0 ± 3.1
Low	70.4 ± 2.8	69.2 ± 3.5
$P_{ET}CO_{2\ hypoxia}$ (mmHg)		
High	40.2 ± 1.7	38.2 ± 1.7*
Low	38.6 ± 1.6	36.4 ± 1.7*

Data ($N = 14$) are mean ± the 95% confidence interval after correction for between-subject variability.
*Denotes significance ($P \leq 0.05$) on post hoc paired data pre- and postflight.

Low ($P = 0.002$) altitude condition (see Table II). However, unlike measures of FIVC, regional (basal) EIT lung volume had not recovered to baseline values at FIVC4. EIT data were only available from 10 and 13 subjects in the High and Low condition, respectively. Loss of data was typically due to improper electrode contact, which was measured as part of the systems signal quality assessment prior to recordings with registration of data only possible if all 16 electrodes presented electrode-to-skin contact impedance below a predetermined threshold.

S_pO_2 was lower postflight than preflight for all of the three oxygen gas mixes inspired ($P < 0.05$), with no differences found between the High and Low cabin altitude conditions (see **Table III**. The lower oxygen saturations resulted in an increase in the estimated pulmonary shunt from 1.9 ± 2.5% to 4.9 ± 3.3% ($P = 0.011$) and from 1.9 ± 2.3% to 5.7 ± 3.3% ($P = 0.003$) in the High and Low cabin altitude conditions, respectively. Changes in the estimated shunt fraction were comparable between the two cabin altitude conditions. V_T and RR were unaffected by exposure to high $+G_z$ flight breathing 60% oxygen following either High or Low cabin altitude sorties. There was also no effect on postflight $P_{ET}O_2$, but $P_{ET}CO_2$ was significantly decreased following both High ($P = 0.021$) and Low ($P = 0.008$) cabin altitude sorties (Table III).

DISCUSSION

This study investigated whether a minimum 60% oxygen (balance 40% nitrogen) breathing induces acceleration atelectasis in pilots during high $+G_z$ flight and explored whether cabin altitude had any influence on the extent of atelectasis identified. This gas mix was chosen because most combat aircraft using onboard oxygen generator technology supply around 60% oxygen to the crew at cabin altitudes where dynamic G_z maneuvering is conducted, so it is representative of real-world conditions.

Change in FIVC was used as the primary measure of atelectasis in this study. Multiple exposures to +5 G_z while breathing 60% oxygen were found to be associated with mean reductions in FIVC of 4.9% (−0.24 L) and 3.8% (−0.17 L) when FIVC1 was compared with the mean preflight FIVC in the High and Low cabin altitude sorties, respectively. These findings are consistent with previous research;[14] one unpublished study reported a 4.3% decrease in FIVC after exposing subjects to 75 s at +4 G_z while breathing 60% oxygen.[11] When using contemporary pilot flight equipment and life support systems, the current study therefore demonstrates that an F_IO_2 of 60% is still sufficient to moderate the development of acceleration atelectasis, although a reduction in lung volume still occurs. As expected, postflight FIVC recovered with successive breathing maneuvers. Symptoms were not formally assessed in the current study, but a cough, or an urge to cough, was seen during postflight FIVCs (illustrated in **Fig. 2**) with relatively few symptoms reported in flight. The reduction in FIVC is attributable to inspiratory limitation, with a loss of inspiratory capacity that broadly matches the reduction in FIVC (rather than loss of functional residual capacity).

Placement of EIT electrodes in this study was used to measure changes within the lower lobes of the lungs,[23] and so, the decrease in magnitude of the impedance change with lung inflation during the postflight FIVCs suggests that there was a reduction in basal lung volume. The fall in $FIVC_{EIT}$ as a percentage of pre-exposure values was much larger than accompanying changes in FIVC (5 vs. 15%) and did not recover to pre-exposure values at FIVC4. This suggests that basal lung regions remain resistant to re-expansion and the discrepancy with normalized estimates of FIVC demands further consideration.

It is possible that the 'recovery' in overall lung volume actually represents recruitment of lung regions known as a Pendelluft phenomenon.[12] Alternatively, artifacts caused by changes in impedance at the electrode-to-skin interface, for example by increased sweating, could be present. However, EIT measures were relative, representing a change from that recorded at residual volume (RV), so any offset in voltage at the electrodes would have largely been negated. EIT derived measures of V_T and FIVC are repeatable,[2,23] but the effects of cabin altitude could not be compared with this technique as identical electrode placements could not be guaranteed on consecutive days. Nevertheless, good correlation was observed between Pre measurements on each test day ($r^2 = 0.87$). EIT data in Table II and Fig. 2 show three FIVC maneuvers of a symptomatic subject pre- and postexposure. The first Post $FIVC_{EIT}$ was approximately 24% lower than Pre and toward the end of inspiration the subject coughed (depicted as a double peak in the impedance trace). FIVC end-expiratory impedance then increased, indicating recruitment of lung tissue clearly visible in the EIT images. Successive FIVC maneuvers were higher but did not recover to preflight values.

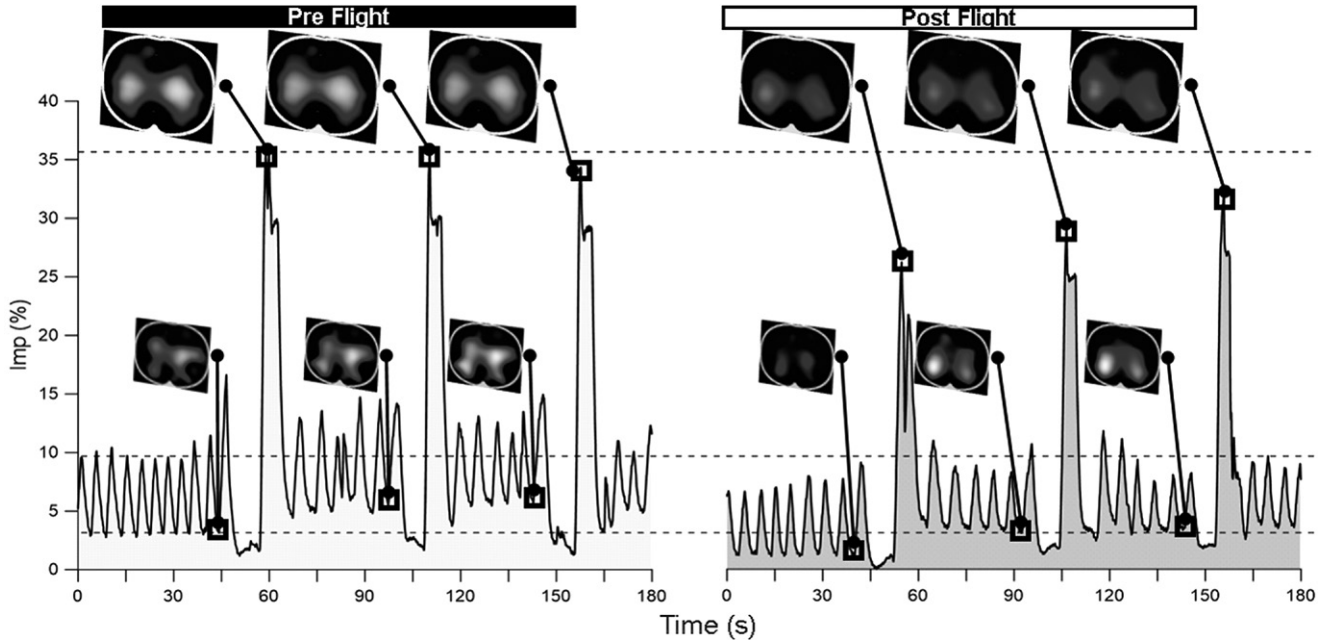

Fig. 2. Images of regional lung impedance acquired by electrical impedance tomography (EIT) over time for the whole image during the performance of three forced inspiratory vital capacity (FIVC) maneuvers (each separated by a period of tidal breathing) performed pre- (left) and postflight (right) in participant 5 (low altitude sortie). The top row of images is that recorded at maximal inspiration and the bottom at the end of a normal breath (i.e., functional residual capacity; FRC). To visualize changes a greater gain was used for images at FRC (×4.5) than at maximal lung volume, therefore comparison of images can only be made within each row. The dashed lines represent the impedance recorded at average end expiration, end expiration plus mean impedance change during tidal breathing, and peak impedance during a maximal breath preflight. Images were referenced as changes from the image recorded at residual volume and thus scales are configured to contrast relative changes in impedance. Note that this subject coughed during the performance of the first FIVC postflight (observed in the impedance trace as a double peak).

The postflight reduction in peripheral arterial oxygen saturation was consistent between subjects under the conditions investigated (Table III). The decrease observed in this study, although highly statistically significant, is modest and unlikely to have operational relevance. It does, however, indicate impairment of blood oxygenation. It is possible that mild atelectasis (as evidenced by the decrease in FIVC) was sufficient to result in a small pulmonary shunt. The reduction in arterial oxygen saturation lends support to the possibility suggested by the EIT data of a persistent functional impairment that is not reflected by overall measures of lung volume. Persistent reduction in arterial oxygen tension has been demonstrated following 75-s exposure to +4 G_z on the centrifuge, providing the subject avoided deep breathing.[10] A flight trial involving a series of maneuvers at +5.5 G_z sustained for 30–40 s over a total sortie duration of 30–40 min has also demonstrated postflight reductions in S_pO_2 (breathing air) that are of similar magnitude to those reported in the current study.[14] These findings suggest compromised lung function and blood oxygenation postflight, possibly due to atelectasis. However, it is widely accepted, and supported here, that the provision of 60% oxygen is sufficient to prevent gross atelectasis formation and will, in any case, provide adequate oxygenation during flight. Further studies using different F_IO_2 may still be required to delineate the mechanism and to determine whether more significant postflight reductions, potentially of operational relevance, occur with higher F_IO_2.

One of the aims of the study was to investigate whether cockpit pressure altitude had a protective effect on the development of acceleration atelectasis. In this study we found no difference in outcomes between flights carried out at cockpit pressure altitudes of 4000 and 18,000 ft (1219 and 5486 m), a maximum difference in barometric pressure of approximately 276 mmHg. It is possible that a different outcome might result with a higher F_IO_2, which could result in greater development of acceleration atelectasis.

In prioritizing consistent +G_z exposures across both conditions, due to performance limitations of the Hawk T Mk1 aircraft, possible order effects could not be controlled out. The statistically significant difference in baseline FIVC on the two flight days indicates that this introduced a systematic, methodological confound, which is nonetheless of interest. Preflight baseline FIVCs were consistently greater on the second day of testing (Low cabin altitude) ($P = 0.036$). It is possible that the initial fit of specific AEA garments may have relaxed following the first sortie and thus afforded greater expansion of the lungs during maximal inhalation. This perhaps warrants further study to examine how garment fit changes with repeated use and if there are implications to G protection. Notably, however, if any slackening of AEA fit did occur, the magnitude of changes in lung volumes during flight was unaffected.

Further limitations of the study, additional to the control of exposure orders, include delays between laboratory measurements and +G_z exposures. Despite endeavors to minimize this

interval, mandatory in-aircraft pre- and postflight procedures could not be shortened. Additionally, a nonflying control condition was not included and, therefore, could not be compared with postflight data. The acceleration exposures were not fully representative of air combat in magnitude or duration but were repeatable and within aircraft capability at both altitudes studied.

The major findings from this study are: a small reduction in postflight lung volume occurred, but recovered with repeated maximal inspirations, suggesting limited development of atelectasis; regional surrogate measures of basal (caudal) lung volume by EIT also decreased but did not recover to preflight values; peripheral arterial oxygen saturation was decreased postflight, suggesting formation of a small (5–6%) pulmonary shunt; and none of the measurements were influenced by cabin altitude. In summary, postflight measurements of FIVC and $FIVC_{EIT}$ indicate that mild degrees of atelectasis can occur following multiple in-flight exposures to +5 G_z while breathing 60% oxygen at low and high cabin altitudes. $FIVC_{EIT}$ data imply that mildly atelectatic regions may not fully resolve with simple postflight breathing maneuvers.

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Aviation Decompression Sickness in Aerospace and Hyperbaric Medicine

Craig J. Kutz; Ian J. Kirby; Ian R. Grover; Hideaki L. Tanaka

INTRODUCTION: The U.S. Navy experienced a series of physiological events in aircrew involving primarily the F/A-18 airframe related to rapid decompression of cabin pressures, of which aviation decompression sickness (DCS) was felt to contribute. The underlying pathophysiology of aviation DCS is the same as that of diving-related. However, based on the innate multifactorial circumstances surrounding hypobaric DCS, in clinical practice it continues to be unpredictable and less familiar as it falls at the intersect of aerospace and hyperbaric medicine. This retrospective study aimed to review the case series diagnosed as aviation DCS in a collaborative effort between aerospace specialists and hyperbaricists to increase appropriate identification and treatment of hypobaric DCS.

METHODS: We identified 18 cases involving high-performance aircraft emergently treated as aviation DCS at a civilian hyperbaric chamber. Four reviewers with dual training in aviation and hyperbaric medicine retrospectively reviewed cases and categorized presentations as "DCS" or "Alternative Diagnosis".

RESULTS: Reviewers identified over half of presenting cases could be attributed to an alternative diagnosis. In events that occurred at flight altitudes below 17,000 ft (5182 m) or with rapid decompression pressure changes under 0.3 atm, DCS was less likely to be the etiology of the presenting symptoms.

CONCLUSIONS: Aviation physiological events continue to be difficult to diagnose. This study aimed to better understand this phenomenon and provide additional insight and key characteristics for both flight physicians and hyperbaric physicians. As human exploration continues to challenge the limits of sustainable physiology, the incidence of aerospace DCS may increase and underscores our need to recognize and appropriately treat it.

KEYWORDS: decompression sickness, aviation, high-performance aircraft, hyperbaric.

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In 2017, the U.S. Navy experienced a significant increase of physiological episodes in aircrew related to rapid decompression of cabin pressures, ultimately leading to an extensive $50 million investigation into hypoxia, decompression sickness, and aircraft maintenance procedures.[14] Although no 'smoking-gun' was reported, a multifactorial approach to pilot safety was developed, including placement of hyperbaric chambers on Nimitz-class aircraft carriers.[10] Since this report, the incidence of physiological episodes has substantially decreased.

The underlying pathophysiology of hypobaric decompression sickness (DCS) is universally felt to be the same as that of diving-related DCS.[2,4] In brief, rapid reductions in ambient pressures result in dissolution of gases in body tissue with subsequent endovascular and tissue trauma and activation of the inflammatory cascade.[4,18,20] Canonically, this is best understood following diving or depressurization of a hyperbaric chamber.[4,19] Less familiar in clinical practice is the identification and diagnosis of altitude, or aviation-related DCS. This unique presentation falls at the intersection of aerospace and hyperbaric medicine, and thus, specialists in each field alike may be less familiar and comfortable in making this diagnosis and managing it. Often emergent referral for recompression to civilian

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chambers are coordinated through military flight surgeons for high-performance aircraft incidents. Yet civilian emergency hyperbaric oxygen chambers may not routinely manage pilots of high-altitude, high-performance aircraft. Alternatively, flight surgeons may not consistently differentiate DCS from other diagnoses or be familiar with hyperbaric chamber operations. Thus, the goal of our study was to collate and revisit presumed aviation-related DCS cases presenting to a civilian emergency hyperbaric chamber over the past decade to further understand the phenomena encountered and better differentiate key characteristics for diagnosis and treatment within this crossroads.

DCS is a clinical diagnosis made through evaluation of a dive (or altitude) profile, predisposing risks, onset of presentation, and manifestation of symptoms to identify and treat this clinical decision.[4,19] In general, DCS symptoms present broadly, manifesting most commonly as musculoskeletal pain, paresthesias, or fatigue; however, serious neurological or cognitive deficits may arise in more advanced cases.[18,25] Hyperbaric oxygen therapy (HBOT) continues to be the gold standard for treatment in severe cases for both hyper- and hypobaric DCS refractory to ground level oxygen and continues to be an AHA level I recommendation.[9,19] HBOT is a multifaceted approach to DCS treatment including immediate bubble volume reduction, increased diffusion differential for tissue inert gases, reduction in inflammatory signaling, ischemic tissue oxygenation, and mitigation of nervous system edema.[4,9,19] In recent years, however, less emphasis has been placed on physical bubble compression.[4,18] To date, documented cases of fatal hyperbaric DCS far outweigh that of hypobaric DCS exposures.[11,21] However, serious morbidity continues to be reported related to aviation or rapid altitude decompression.[12] High-performance aircraft pilots, such as fourth- and fifth-generation fighter jets and legacy aircraft such as the U-2, continue to be the vast majority of cases and can present with mission- or career-ending pathology.[1,3,10]

The University of California-San Diego (UCSD) Hyperbaric Medicine Center is the only 24-h emergency treatment hyperbaric chamber in the southern-most end of California. It is within close proximity of two military air bases in San Diego, CA, USA, and thus was involved in the diagnosis and treatment of a series of aviation-related incidents from 2010 to 2020. This retrospective, single-center case series aimed to review the chain of diagnosed aviation DCS in an effort to appropriately identify and treat aviation DCS. Although this study was not aimed to fully elucidate the pathophysiology of aviation DCS, our goal was to provide better understanding of key features in patient presentation for both flight physicians and hyperbaricists alike.

METHODS

Approval was obtained from the UCSD Institutional Review Board (protocol #800207) for this retrospective analysis for all cases used in this study. No written consent was required per university and Institutional Review Board ethical guidelines.

Utilizing a case series, cross-sectional study design, we retrospectively collected medical records using EPIC Slicer Dicer and logbooks of the UCSD multiplace hyperbaric chamber billing ICD 10 codes: Caissons Disease Decompression Sickness (T70.3) or Air Gas Embolism (T79.0XXA). From August 2010 to August 2020, 21 cases were seen at an academic, multiplace hyperbaric chamber in San Diego and involved altitude or aviation technology (e.g., skydiving, high-performance aircraft, hypobaric chamber). This 24-hour emergency treatment hyperbaric chamber is located approximately 12 mi from the Marine Corps Air Station Miramar (KNKX) and approximately 3 mi from Naval Base Coronado's North Island Naval Air Station (KNZY). In addition, the UCSD Hyperbaric Medicine Division provides treatment for various cases from the southwestern United States and Hawaii. Recompression treatment tables used were determined by fellowship-trained, board-certified Undersea and Hyperbaric Medicine physicians, with additional hyperbaric oxygen treatments determined on a case-by-case basis until maximum improvement of symptoms was observed. Initial diagnosis was based on case presentations, symptoms, circumstances of flight, and coordination with local military commanding officers and flight surgeons.

Of the 21 cases in our retrospective case series, 1 case was excluded in which a mechanic was on ground level with rapid pressurization and decompression of an F/18 cabin. Two additional cases were excluded from our DCS case series due to diagnosis by original provider as "Air Gas Embolism". Two pilots were seen for two separate events and deemed to represent two unique presentations. The data collected retrospectively included age, sex, military service, symptoms, flight ceiling, altitude at time of the decompression event as reported by the flight surgeon or patient, cabin pressure, time from the decompression event to onset of symptoms, time from the decompression event to presentation to UCSD's Hyperbaric Medicine Division, use of ground level oxygen, treatment profiles, additional treatments, and outcomes. Flight details provided at time of presentation to an emergency room were limited to information within the public domain. In some cases, altitudes of decompression were unknown and were listed as 'unknown decompression event'. Pressures at altitude were approximated and normalized with an assumption of 15°C as specific barometric pressure and temperature during flights were not collected.

Cases were independently and retrospectively reviewed by physicians experienced in both aviation medicine and hyperbaric medicine, including one civilian physician, two former military flight surgeons (U.S. Air Force and U.S. Navy), and one active Canadian Armed Forces physician. All reviewers were fellowship trained in Undersea and Hyperbaric Medicine. Individuals were provided standardized summary reports for each case and required to identify a nominal designation as: 1) "Decompression Sickness"; or 2) "Alternative Diagnosis Favored" (**Fig. 1**). Each reviewer was then required to list key presentations, symptoms, or flight details in each case that led to their specific outcome. These features were then collated for assessment related to the diagnosis.

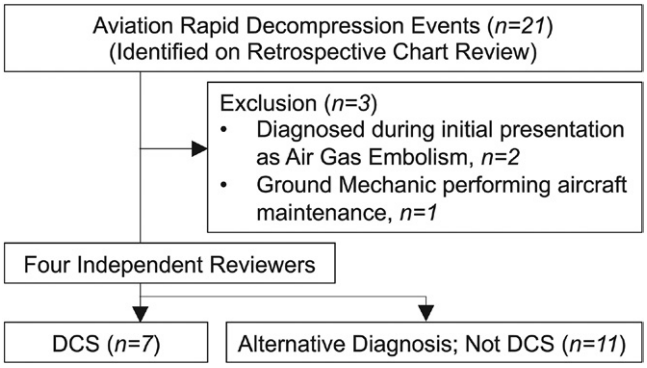

Fig. 1. Flow chart for patient selection and inclusion and exclusion criteria for study. DCS, decompression sickness.

Statistical Analysis

Data, when applicable, was expressed using descriptive statistics for parametric variables and frequencies and percentages for nonparametric variables. Two-tailed Chi-squared/Fisher's exact test was used to identify significant variables ($P < 0.05$). Analysis was performed with GraphPad Prism 9 v. 9.3.1 (GraphPad Software, San Diego, CA, USA) and MedCalc Software Ltd, v 20.027 (MedCalc Software Ltd, Ostend, Belgium). A threshold of P-value < 0.05 was used for statistical significance. Outliers were identified using modified z-scores and Grubbs test, or extreme studentized deviate.

RESULTS

Over a 10-year period, 21 cases of aviation-related rapid decompression events were treated at the UCSD Hyperbaric Medicine Division in San Diego, CA, USA. Of those, 18 cases were diagnosed at time of presentation by fellowship-trained and board-certified hyperbaric physicians as "Decompression Sickness". The patient demographics are outlined in **Table I**.

Of the total cases reviewed retrospectively for this study, seven cases were thought by at least one reviewer to represent DCS based on history, physical exam, and circumstances of the flight. All 18 cases in this study were comprised of patients from government branches, including U.S. Navy, U.S. Marine Corps, foreign military army, and the National Aeronautics and Space Administration (NASA). Airframes primarily included the McDonnell Douglas F/A-18 Hornet, a twin-engine supersonic fighter and attack jet with multi-person cockpit configuration. Other aircraft included the McDonnell Douglas and Boeing F/A-18E Super Hornet, a twin-engine multirole fighter jet with single- or two-seat configuration and advanced derivatives to the F/A-18, and the Northrop T/38 Talon twinjet supersonic jet trainer. One case involving a high-performance airframe also included exposure to a high-altitude hypobaric chamber as an inciting factor. Additionally, one case of an aviation-related event involved a high-altitude military parachutist involved in high altitude-high opening (HAHO) free fall. Presenting symptoms and key physical exam findings are outlined in **Table II**. All of the cases were initially diagnosed and treated as DCS within a civilian multiplace chamber using U.S. Navy treatment tables at time of presentation (**Fig. 2**).

Table I. Demographics of Aviation Decompression Events Including Military Service and Airframes.

	REVIEWER DCS	ALTERNATIVE DIAGNOSIS	TOTAL
Age			
N	7	11	18
Mean (std)	35.1 (6.84)	31.8 (4.49)	33.1 (5.58)
Median	36	31	32
Range	26-45	26-42	26-45
Gender, *N* (%)			
Male	6 (85.7)	11 (100)	17 (94.4)
Female	1 (14.3)	--	1 (5.6)
Military Service, *N* (%)			
U.S. Navy	3 (42.9)	3 (27.3)	6 (33.3)
U.S. Marines	3 (42.9)	7 (63.6)	10 (55.6)
U.S. Army	-	1 (9.0)	1 (5.6)
Other	1 (14.3)	--	1 (5.6)
Airframe, *N* (%)			
F/18	6 (85.7)	8 (72.7)	14 (77.8)
F/18 Super Hornet	--	2 (18.2)	2 (11.1)
T/38, Other	1 (14.3)	--	1 (5.6)
HAHO	--	1 (9.0)	1 (5.6)

DCS, decompression sickness; HAHO, high altitude high opening.

This retrospective review by a panel of experts in aviation medicine and hyperbaric medicine identified specific cases felt to represent DCS based on circumstances of presentation. Cases felt by at least one reviewer to be most consistent with decompression sickness as etiology of presentation represented 7 of 18 cases, or less than half. Notably, only two of the cases, or 11.1%, were unanimously agreed to be DCS by all four reviewers (**Table III**).

Consistently, subjects were described as "feeling drunk or hung over". After retrospective review, there was no significant difference between cases felt to represent DCS vs. alternative diagnosis in subjective symptoms, including joint pain, fogginess, confusion, or paresthesias. Primarily, physical exam findings that endorsed objective presentations were more likely to be favored by reviewers as DCS, including neurological deficit, coordination abnormality, or decline in cognitive function.

In the subgroup of DCS cases, a change in pressure during rapid decompression equivalent to at least 0.3 atm (χ^2, P-value <0.05, CI 95%) reflected statistically significantly increased risk that the presentation represented DCS. For example, Case 1 in Table III was judged by all four reviewers to be consistent with DCS. The pilot experienced a change in pressure of 0.38 atm, resulting from three rapid decompression events from a cabin pressure of 8000 ft (2438 m; approximately 0.75 atm at 15°C) to 26,000 ft (7925 m; approximately 0.37 atm at 15°C). To the contrary, Case 8 (not listed) was unanimously judged to favor an alternative diagnosis for symptoms. This pilot experienced a change in pressure of 0.19 atm resulting from decompression events in a cabin pressure of 5000 ft (1524 m; approximately 0.83 atm at 15°C) to 12,000 ft (3658 m; approximately 0.64 atm at 15°C). In fact, in cases judged by at least one reviewer to be

Table II. Symptoms and Physical Exam Findings in Subgroup Analysis for Decompression Sickness vs. Alternative Diagnosis.

	DECOMPRESSION SICKNESS			ALTERNATIVE DIAGNOSIS		
	No.	DCS (%) *(N = 7)*	TOTAL (%) *(N = 18)*	No.	DCS (%) *(N = 11)*	TOTAL (%) *(N = 18)*
Joint Pain	5	71.4	27.8	5	45.5	27.8
Fogginess	3	42.9	16.7	8	72.7	44.4
Difficult Concentrating	3	42.9	16.7	3	27.3	16.7
Lightheaded	2	28.6	11.1	2	18.2	11.1
Headache	2	28.6	11.1	5	45.5	27.8
Speech Abnormality	2	28.6	11.1	1	9.1	5.6
Paresthesias	2	28.6	11.1	7	63.6	38.9
Myalgias	2	28.6	11.1	2	18.2	11.1
Gait Instability	2	28.6	11.1	0	-	-
Pruritits	1	14.3	5.6	0	-	-
Vertigo	1	14.3	5.6	0	-	-
Rash	1	14.3	5.6	0	-	-
Fatigue	1	14.3	5.6	1	9.1	5.6
Vision Changes	0	-	-	3	27.3	16.7
Tinnitus	0	-	-	1	9.1	5.6
Shortness of Breath	0	-	-	1	9.1	5.6
Loss of Conscious	0	-	-	1	9.1	5.6
Chest Pain	0	-	-	1	9.1	5.6
Neurological Deficit	3	42.9	16.7	0	-	-
Coordination/Gait Deficit	2	28.6	11.1	0	-	-
MMSE < 30	3	42.9	16.7	0	-	-

MMSE: Mini-Mental State Exam.

consistent with DCS, the change between flight altitude pressure and rapid decompression pressures exceeded 0.3 atm (**Fig. 3**).

Additional flight data, as shown in **Table IV**, indicates that if the maximum altitude of the airframe was equal to or below 17,000 ft (5182 m) during the rapid decompression event, the reviewers were less likely to agree upon the diagnosis being decompression sickness with 95% confidence (χ^2, *P*-value <0.05). However, this strength of association was not significant for the cabin decompression altitude reported [*P*-value 0.266, CI 95% equal to or above 15,000 ft (4572 m)]. Thus, in general, a rapid decompression event required at least a maximum flight ceiling of 17,000 ft for sufficient pressure differentials in cabin pressure to favor decompression sickness as the plausible etiology for symptoms.

DISCUSSION

Aviation or hypobaric DCS is encountered less frequently than diving DCS, most likely because civilians have less access to high-performance military flights and unpressurized high-atmosphere sorties. Often, recognition and treatment are a collaborative effort between flight surgeons and hyperbaric physicians, yet circumstances in presentations may still lay outside of individual medical subspecialty expertise. Confounding the diagnosis is less familiarity and exposure to military operations and high-performance technology by the civilian physicians involved in care.

DCS continues to be a clinical diagnosis. Multiple attempts at predictive models date back to as early as 1908.[4,5] These early

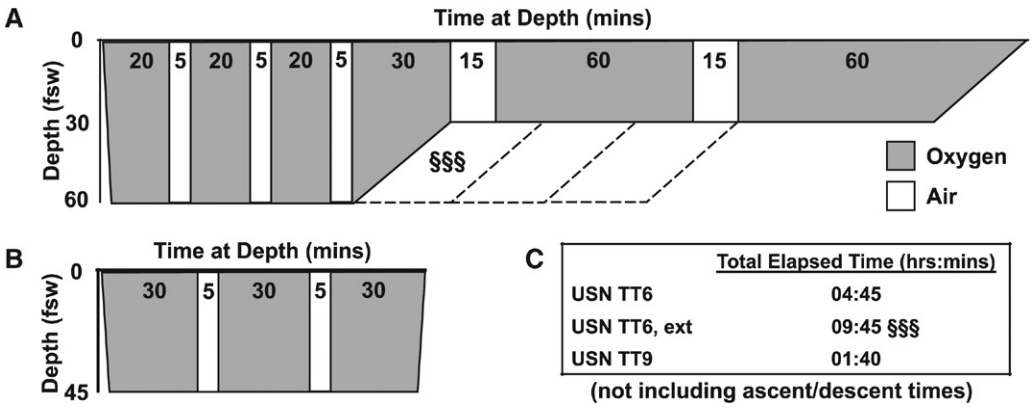

Fig. 2. U.S. Navy Treatment Tables for decompression sickness showing total time allocated for each treatment. A) U.S. Navy Treatment Table 6 (USN TT6) with possible extension (§§§) of treatments to a total of 585 min outlined with dotted lines [i.e., every one extension (ext) at 60 feet of sea water (fsw) adds an additional three 20-min oxygen periods with two 5-min oxygen breaks at 30 fsw]. B) U.S. Navy Treatment Table 9 (USN TT9). C) Duration in hours:minutes of each table.

Table III. Selected Cases That Reviewers Felt Represented Decompression Sickness.

PATIENT DATA; AIRFRAMES	AIRCRAFT ALTITUDE (ft)	CABIN ALTITUDE (ft)	DECOMPRESSION ALTITUDE (ft); [NO. EXPOSURES]	PRESSURE CHANGE (atm)	PRESENTATION	TREATMENT
Number of Reviewers Favor DCS (4 of 4)						
Case						
1) 40-year-old male pilot F/18	29,000	8,000	26,000 [3]	0.38	Symptoms: fogginess, lightheaded, headache, abnormal speech, confusion Onset: at altitude Exam: MMSE <30	TT6
15) 45-year-old female pilot; Hypobaric Chamber; Pressure Suit; T/38 (+12-hours)	65,000 25,000	35,000 13,000	Unknown N/A	0.94	Symptoms: joint pain, myalgias, paresthesias Onset: >1 h on the ground; at altitude Exam: sensation deficit	TT6, ext TT9
Number of Reviewers Favor DCS (≥1 of 4)						
Case						
3) 36-year-old male pilot F/18	35,000	8,000	16,000 [>10]	0.2	Symptoms: fogginess, speech abnormality, focal extremity weakness, gait instability, difficulty concentrating Onset: ≤1 h on the ground Exam: MMSE <30, neurological deficit, gait deficit	TT6 TT6, ext TT9 TT9
5) 26-year-old male pilot F/18	23,700	8,000	23,700 [1]	0.35	Symptoms: paresthesias, joint pain Onset: >1 h on the ground Exam: no pertinent findings	TT6
12) 39-year old male pilot F/18 F/18 (+48-hours) F/18 (+24-hours)	 1,000 22,000 22,000	 1,000 8,000 8,000	 33 fsw [30] 33 fsw [10] n/a	1.26	Symptoms: nausea, myalgia, headache, vertigo, rash, fogginess, confusion Onset: at altitude, >1 h on the ground Exam: MMSE <30, positive sharpened Romberg	TT6 TT5
13) 28-year old male pilot F/18	22,000	8,000	20,000 [1]	0.28	Symptoms: joint pain, lightheadedness Onset: at altitude Exam: no pertinent findings	TT6
17) 32-year-old male pilot	16,000	8,000	15,000 [1]	0.18	Symptoms: fatigue, joint pain Onset: >1 h on the ground Exam: sensation deficit	TT6

Flight profiles, changes in cabin pressure for given rapid decompressions, and presenting symptoms and exam findings, as well as treatments, are listed.
DCS, decompression sickness; MMSE, Mini-Mental State Exam; TT, United States Navy Treatment Table; ext, extensions; fsw, feet of sea water.

decompression models by physiologist Haldane provided early diving tables and described a theoretical "2:1 supersaturation" ratio.[5] Essentially, a pressure differential of 2:1 was required for inert gas saturated in tissues to exceed environmental pressures. This early model has been adapted multiple times and hyperbaric medicine still traditionally teaches that the threshold for developing diving DCS must exceed approximately 20 fsw, or a pressure differential of 0.6 atm.[4,19,24] However, the unique environment and circumstances associated with aviation DCS makes this model difficult to extrapolate. The U.S. Air Force compiled a large database on over 3000 subject exposures in a hypobaric chamber to develop an Altitude Decompression Sickness Risk Assessment Computer (ADRAC).[22,26] In this report, sigmoidal regression indicated development of venous gas embolism (VGE) at as low as 12,000 ft (3658 m); however, incidence of DCS threshold was approximately 16,000 ft to 18,000 ft (4877 to 5486 m).[26] Conkin et al. also published probabilistic DCS models to encompass a wider range of DCS incidence, including high altitude hypobaric environments.[7] Yet, due to the inherent multifactorial presentation and unknown confounders in high-performance aircraft, aviation DCS continues to be difficult to diagnose and models in DCS theory are still lacking.

Our study identified 18 events diagnosed and treated as aviation DCS over the past decade ranging from 2010 to 2020. As Table II and Table IV show, the presentations, symptoms, and flight circumstances were broad. Our retrospective review involved four independent civilian and military reviewers with dual backgrounds in hyperbaric and aerospace medicine, with the goal of differentiating key characteristics in the presentation that may assist in the diagnosis. Reflective of the difficulty in diagnosing aviation DCS, only two cases in our entire series were unanimously felt to be attributed to DCS (Table III). Less than half of the total cases were felt to represent DCS by at least one reviewer, likely reflecting both the

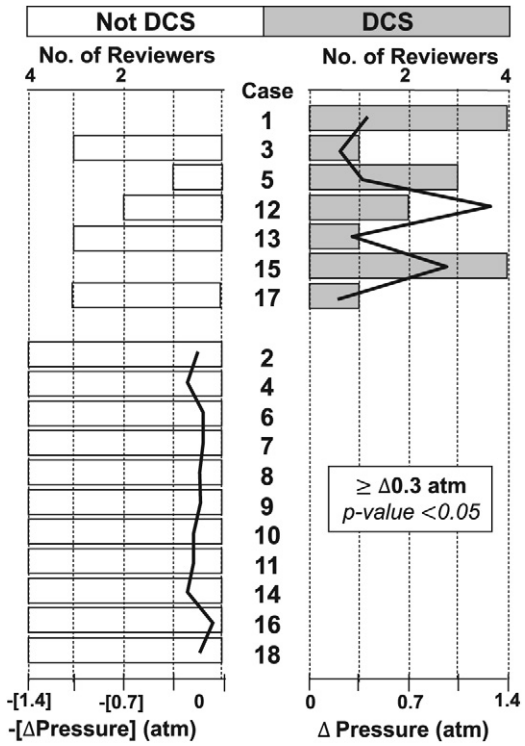

Fig. 3. Number of reviewers designating DCS vs. alternative diagnosis (Non-DCS). Reviewers reported as nominal values. Pressure changes from cabin altitude to decompression altitude for each case reported as change in pressure (atm). Right sided indicates changes in pressure for cases diagnosed as DCS by at least one reviewer. Left sided (reported as inverse values) indicates changes in pressure of cases that no reviewers felt was DCS. This figure excluded one outlier based on his flight profile experiencing brief episodes below sea level due to overpressurization, making his flight profile brief hyperbaric conditions. *P*-value based on 95% CI; Δ, change; DCS, decompression sickness.

difficulty and unfamiliarity in diagnosis by typical civilian hyperbaric physicians at time of presentation. Alternative diagnoses considered included (but were not limited to) hypoxia, air gas embolism, trauma, contaminated gas, non-biological, or substance withdrawal.

In this case series, all were treated with recompression therapy, as at the time of presentation they were felt to represent clinically significant aviation DCS. Although no complications were experienced during this series of treatments, the risk-benefit of recompression in coordination with resource management is not trivial. The U.S. Navy Diving Manual recommends treatment of DCS with Treatment Table 6, a recompression profile with a duration of 285 min, with a maximum possible duration of 585 min if extensions are required (Fig. 2).[15] Further, six cases were admitted to the inpatient hospital for residual symptoms or continued monitoring, of which only three were judged to be aviation DCS by at least one reviewer. Significant resource allocation and evacuation to recompression chambers are used for the diagnosis of DCS with continued symptoms despite ground level oxygen.[20] Alternative treatments have been proposed, but are still not universally adopted.[6,8] Aviation DCS remains a high-profile concern for military and governmental authorities.[3,9,13] Thus,

Table IV. Flight Profile Including Maximum Altitude, Changes in Pressure, Decompression Altitude, and Timing for Onset of Symptoms for Both DCS and Alternative Diagnosis (Non-DCS) Cases.

	REVIEWER DCS No. (*N* = 6)	ALTERNATIVE DIAGNOSIS No. (*N* = 11)	χ^2 *P*-VALUE
Δ Altitude Pressure (atm)			
≥0.3	3	0	<0.05*
Maximum Flight Altitude (ft)			
≤17,000	1	9	<0.05*
Decompression Altitude (ft)			
≥18,000	4	7	0.900
≥15,000	6	9	0.266
Symptom Onset			
≤1 h on the ground	1	7	0.064
>1 h on the ground	3	2	0.169
In flight	2	2	0.482

Case 15 was excluded from calculations due to extremes in altitude experienced.
DCS, Decompression Sickness; Δ, Change; χ^2, Chi-squared.
*Significant.

a formal diagnosis of DCS can be career altering, as such with Navy divers, where a neurological DCS event can permanently disqualify from future missions.[15] Alternatively, in our case series, we identified multiple events where an alternative differential diagnosis should have been considered. For instance, Case 16 was unanimously felt to represent possible substance withdrawal, such as alcohol, due to a toxicological syndrome of tongue fasciculations, tremors, and tachycardia—symptoms traditionally inconsistent with DCS.[4,19] Noting the low number of cases overall, sample bias can limit conclusions taken from this study; however, the consideration of alternative management of presentations other than DCS should be deliberated. These cases reinforce our need to better understand proper identification of aviation DCS.

The underlying mechanism behind aviation DCS is complex. In fact, the underlying propagation of DCS or arterial gas embolism (AGE) in diving continues to be of some debate amongst hyperbaric physicians, despite reports of DCS as early as the 1840s.[15,18,23] Thus, we attempted to simplify key features in cases felt to favor DCS in an attempt to assist recognition and diagnosis. For instance, we found that objective physical exam findings such as neurological deficits, coordination abnormalities, or cognitive delays favored DCS (Table III). In addition, Fig. 3 shows exposure to change in pressure during rapid decompressions of greater than or equal to 0.3 atm favors DCS. This case series indicates the maximum altitude of flight below 17,000 ft (5182 m) is less likely to be diagnosed as DCS, which is in agreement with prior U.S. Air Force studies.[22,26] Certainly inherent confirmation bias in altitude (i.e., reviewers trained in identifying 18,000 ft/5486 m as a minimum altitude to develop DCS) could skew this simplification in flight altitude for aviation DCS. However, this finding, in coordination with changes in pressures, gives a good foundation for both civilian and military to consider broader differentials with cases presenting outside of these parameters.

As with diving DCS, not one single test or historical presentation can formally make the diagnosis and, to date, the underlying propagation of disease continues to be of some debate.[18] There is still more to learn about aviation DCS. The underlying pathophysiology is complex. In flight, the differential diagnosis is wide and not readily appreciated, as evidenced by the findings in the Navy root-cause analysis of physiological events experienced by aircrew in the last decade.[10,14] Alternative pathophysiology in aviation DCS has included oscillations in pressure of the central nervous system from rapid decompression-recompression, which may mimic traumatic brain injury from blasts, or through alveolar barotrauma from substantial rapid high-altitude decompression.[16,17] Regardless, research is limited and more needs to be performed.

In conclusion, this study is not meant to identify the underlying pathophysiology or cause of aviation DCS, as the sample size ultimately limits any major conclusions. In addition, retrospective reviews of charts inherently induce bias or limitations based on the limited information provided. However, key associations in flight profile showed significant likelihood in agreement for diagnosis of DCS. Flight altitudes under 17,000 ft (5182 m) or reported differential cabin pressure changes less than 0.3 atm during rapid decompression should raise the consideration of an alternative diagnosis for the presenting symptoms.

Aviation physiological events continue to be multifactorial and difficult to diagnose, in particular as it relates to DCS. Aviation DCS overlaps the subspecialty fields of aerospace and hyperbaric medicine. This study aimed to better understand this phenomenon and provide additional insight and key characteristics for both flight physicians and hyperbaric physicians to utilize. As human exploration continues to challenge limits of sustainable physiology, such as space exploration, the incidence of aerospace DCS will increase and underscores our need to recognize and properly treat it.

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Test Pilot and Airline Pilot Differences in Facing Unexpected Events

Yiyuan Zheng; Yanyu Lu; Yuwen Jie; Zhiqiang Zhao; Shan Fu

BACKGROUND: Unexpected events in flight might decrease the transparency of the flying process and weaken the pilot's perception of the current state, or even erode manipulating skills. However, during the flight test of a new or modified aircraft, to verify the boundaries of aircraft aerodynamic performance and handling stability, unexpected events may be encountered that need to be handled by the test pilot. Therefore, studying the differences between test pilots and airline pilots could help improve flight safety.

METHODS: Two kinds of physiological parameters, eye blink rate and average fixation duration and task-related performance of test pilots and airline pilots, were analyzed in three abnormal scenarios. A total of 16 pilots participated. The study was carried out in an A320 flight simulator.

RESULTS: The differences were significant for both test pilots and airline pilots in eye blink rate and average fixation duration. Furthermore, the reaction time of test pilots (Mean = 23.38 s) was significantly shorter than airline pilots (Mean = 42.63 s) in Unreliable Airspeed condition, and the pitch angle deviations between them were significant in both Wind Shear and Unreliable Airspeed condition.

DISCUSSION: The uncertainty of environmental change could create more severe pressure and mental workload influence than actual system failure. For airline pilots, compared with test pilots, the importance of practicing manual flight should still be emphasized. Improving reactions to unexpected ambient conditions and unannounced fault status could also contribute to flight safety.

KEYWORDS: test pilots, airline pilots, flight performance.

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The increased use of advanced techniques and automated systems has not only reduced pilot's workload, but also improved aviation safety remarkably. For instance, the implementation of head-up displays significantly enhances the pilot's situational awareness during takeoff and landing under night flight conditions or flying in bad weather with poor visability.[24] Moir and Seabridge reported the integrated module avionics system provides a more concise display mode and more reasonable alarm logic, making it easier for pilots to operate and monitor the aircraft.[14] However, even for well-trained airline pilots, as Landman et al. stated, excessive automation may decrease the transparency of the flying process and weaken the pilot's perception of the current state, which may lead to automation surprises.[12] Moreover, the extensive use of automation may erode the pilots' manipulating skills. Plenty of aircraft accident reviewers have reported situations in which pilots encountered abnormal automation events. The latest disasters of Lion Air Flight 610 and Ethiopian Airlines flight 302 in 2018 and 2019, respectively, both revealed the flight crews were unable to effectively recognize and respond to undesired multiple airplane automated nose-down stabilizer trim movement and the effects of potential Angle of Attack (AOA) sensor failure.[20]

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Therefore, the novel technology and sophisticated automation design features must be subjected to strict airworthiness certification to ensure safety, as Wise and Hopkin suggested.[28] A large number of compliance activities need to be carried out in the validation and verification stage. The most commonly used methods of compliance (MOC) defined in airworthiness regulations are flight test (MOC 6) and simulator test (MOC 8).[26] Flight test is a kind of compliance activity which obtains and analyzes the required data through the test aircraft flying under real atmospheric scenarios and evaluates the design specifications and safety level of the aircraft.[3] Normally many boundary conditions of aircraft aerodynamic performance and handling stability characteristics should be verified by flight test. For instance, it needs to be demonstrated by flight test that Vlof (Liftoff Speed) shall not be less than 110% of Vmu (Minimum Unstick Speed) in full engines, and 105% of Vmu in single engine shutdown. In general, Perkins indicated that flight test is the preferred method to show compliance rather than simulator test, unless the demonstration is too risky, or the required environment or airplane conditions are too difficult to attain.[17]

Typically, for a newly designed aircraft, the test flight usually takes over 3000 flight hours, and even for a modification model, the duration lasts often more than 1000 h. Thus, it requires test pilots' participation to perform test flights in a relatively short period of time, and not all airline pilots are qualified or capable of completing a flight test. Test pilots, as Culick suggested, refer to the personnel who conduct specific maneuvering flight in a novel or modified aircraft, play an important role in the flight test certification.[5] They evaluate the flight performance and verify the compliance of specific airworthiness standards through acquiring measurement parameters. The minimum entry criterion for a test pilot is to reach the flight instructor level with no less than 7000 flight hours of route operating experience. In addition, he/she must complete a professional training course lasting 50 wk at a qualified test pilot school.[9] Meanwhile, to maintain the qualification, test pilots must satisfy the experience requirements of instrument flight and night flight.

Many studies have investigated the impact of expertise on pilots' physiological characteristics and their flight performance. Undoubtedly, expertise casts light on establishing and maintaining situation awareness in the face of automation surprises or unexpected events. Kasarskis et al. found during VFR flight, experts had obviously shorter dwell times and more total fixations than novices.[11] Similar results were also found in glideslope control and dynamic target tracking tasks where experienced and novice pilots differed in scanning strategies and areas of interest.[10] Furthermore, Tsang identified expert pilots were also able to direct their attentions in a manner conducive to selecting flight-relevant diagnostic information.[27] Endsley expressed more expert pilots made better decisions, such as the future flight state projections, based on current aircraft attitude and speed.[7] However, for routine operations or frequent faults in actual flight, the difference is insignificant. Casner et al. found when abnormal events were presented in a familiar context, reactions were consistent with accepted standards and varied little from pilot to pilot.[2] Nevertheless, to our knowledge, rare study has experimentally examined the behavior of test pilots when facing the unexpected events in flight.

To establish more optimized coping strategies for unexpected events or automation surprises, and more effective training/retraining planning, we studied the differences between test pilots and commercial airlines pilots in their physiological characteristics and flight performance in three abnormal scenarios, including: Encountering Wind Shear after lifting off, Unreliable Airspeed during taking off, and Stabilizer Trim Failure during approach. In each scenario, two kinds of physiological parameters, eye blinks rate and average fixation duration, and task-related performance were analyzed. The experiment was carried out in a D-level A320 flight simulator, using 16 subjects–8 test pilots and 8 airline pilots.

METHODS

Subjects

For this study, 16 Chinese male pilots (8 test pilots and 8 airline pilots), ranging in age from 36 to 52 (Mean = 45.3 ± 4.96), participated. The mean total flight hours of those pilots were 8967 ± 3465 (range from 3000 to 15,000). Among them, eight test pilots, three from Civil Aviation Administration of China (CAAC) and five from Commercial Aircraft Corporation of China, ranged in age from 44 to 50 (M = 46, SD = 2.90), with average total experience of 10,682 h (SD = 2937). The other eight pilots, with 42.5 yr (SD = 5.24) average age and 7252 h mean flight experience (SD = 3275), were all from China Eastern Airlines. Furthermore, each pilot had been captain of Airbus 320, and simultaneously some of them had been recruited as captains for some other types of aircrafts (3 for A330, 2 for A350, and 2 for A380). Before the experiment, all subjects signed the consent form, which was approved by the Institutional Review Board of Shanghai Jiao Tong University.

Equipment

The experiment was carried out on one A320 D-level full flight simulator, which belonged to CAAC in Shanghai, China. The flight simulator conformed to the guidance published in Federal Aviation Administration Advisory Circular AC 120-40B (Airplane Simulator Qualification).[8] The flight simulator had also been used as pilot training and other airworthiness technology research. The checklist, quick reference handbook, and simulator configuration were provided to the pilots. In addition, one head-mounted eye tracker (Tobbi Glass III, Sweden) was used in this study to capture the required data of each subject's dominant eye. The eye tracker was calibrated by instructing participants to gaze at one fixed point before the experiment. Horizontal and vertical eye movement trajectories were interpolated to determine fixation point with a resolution of approximately less than 0.2 cm. The sample of the eye tracker was 100 Hz.

Procedures

For the sake of investigating the tests pilots and commercial airlines pilots' differences, three abnormal scenarios were designed, including Encountering Wind Shear after lifting off (WS), Unreliable Airspeed during taking off (UA), and Stabilizer Trim Failure during approach (STF). The relevant tasks configurations and the procedures of the crew operating are listed below.

Encountering Wind Shear After lifting off. This flight task was conducted in Shanghai Pudong International Airport. The task was initiated when the TOGA (Takeoff/Go-around) button was pressed. Then, the pilot increased the thrust and kept accelerating until the aircraft reached the speed of V1 (takeoff decision speed). Simultaneously, one moderate predicted wind shear at 400 feet was settled. When the corresponding alter appeared, the pilot was required to push the throttle to the maximum position immediately and rotate at the speed of VR. Subsequently, he should increase the pitch angle and maintain it at 18° until getting rid of wind shear (2000 ft). In this scenario, the reaction time to wind shear and pitch angle deviation during the climb were selected to reflect the pilot performance.

Unreliable Airspeed During taking off. This flight task was carried out in Shanghai Pudong International Airport. The pilot performed takeoff and initial climbing according to the standard operation procedures. At an attitude of 5000 ft, total pitot blockage occurred, resulting in unreliable airspeed. The pilot needed to recognize the current airspeed was inconsistent with the state of the aircraft, adjust the thrust, and maintain the height until the airplane reached the target pitch angle corresponding to Flight Crew Operating Manual (FCOM). Subsequently, he was required to keep climbing manually to 20,000 ft according to the weight and center of gravity of the aircraft and the appropriate pitch angels at different flight levels in FCOM. In this scenario, the response time to the unreliable airspeed and pitch angle deviation during the climbing was selected to reflect the pilot performance.

Stabilizer Trim Failure. This task was carried out during the approach phase (Position: PDL, N31 07.8, E121 40.3), and the terminal point was runway 35R in Shanghai Pudong International Airport. The initial status of aircraft in this task was 210 kts speed, 8900 ft altitude, and 168-degree heading. Then, a failure of horizontal stabilizer jamming was set, and the primary flight control system was degraded to the direct mode. Meanwhile, one 'STAB FAULT' warning appeared on EICAS display instantly.

The pilot performed a manual trim by pressing STAB TRIM to try to restore the failed state. After an invalid attempt, he pressed the CUT OUT button to switch off the stabilizer trim tunnel, and adopted the current speed as maximum flight speed and VRef Full +15 kt as reference landing speed to land the airplane with a 3-detent flaps configuration. In this scenario, the reaction time to the alert, and the deviation between actual landing speed and reference speed was selected to reflect the pilot performance.

The research subjects were in the pilot flying role from the left seat. The experiments were carried out from 8:00 a.m. to 4:00 p.m., local time, and all the participants reported being well rested. Each pilot was involved for a maximum of 2 h. Before the experiment, each subject was trained with normal flight profile for half an hour to become familiar with the simulator configurations and the procedures, and was instructed to deal with the unexpected events based on alarm system, display information, and FCOM in the formal test. An experienced A320 type rated flight instructor acted as the nonflying support pilot.

Statistical Analysis

SPSS 17.0 for Windows was used to process the experiment data. ANOVA analysis was implemented in this study. When $P < 0.05$, the results were considered statistically significant.

RESULTS

The results of the experiment would be described in two dimensions. Due to individual differences, physiological parameters would be analyzed considering same subjects. On the other hand, the flight performance of two types of pilots would also be compared based on different trials.

Eye Blink Rate

For test pilots, the difference was significant ($F(2, 21) = 5.799$, $P = 0.010$) in three scenarios. In UA, the average eye blinks rate was maximum (Mean = 12, SD = 2.62), followed in STF (Mean = 11.25, SD = 2.49), and the minimum was in WS (Mean = 8.13, SD = 2.10). Further, post hoc tests showed a significant difference between WS and UA ($P < 0.01$), and between WS and STF ($P = 0.017$). For airline pilots, most results of eye blinks rate were similar. The most frequent average blink rate was found in UA (Mean = 10.63, SD = 2.13), then in STF (Mean = 8, SD = 1.77), and the least was in WS (Mean = 7.88, SD = 1.55), as shown in **Fig. 1**. The difference was also significant [$F(2, 21) = 5.726$, $P = 0.010$]. However, post hoc tests showed a significant difference between WS and UA ($P < 0.01$), and between UA and STF ($P < 0.01$).

Average Fixation Duration

Considering average fixation duration in three abnormal events, the results of test pilots and airline pilots were similar. The minimum average fixation duration both occurred in STF, which was 1.77 s (SD = 0.35) and 2.19 s (SD = 0.26) respectively. The medium duration was in UA, which was 2.12 s (SD = 0.24) and 2.33 s (SD = 0.18) separately, and the maximum duration appeared in WS, which was 2.46 s (SD = 0.26) and 2.63 s (SD = 0.22), as shown in **Fig. 2**. In addition, the difference is significant for both test pilots ($F(2, 21) = 11.519$, $P < 0.01$) and airline pilots ($F(2, 21) = 8.614$, $P < 0.01$). For test pilots, post hoc tests showed a significant difference between WS and UA ($P = 0.028$), WS and STF ($P < 0.01$), and between UA and STF ($P = 0.024$). However, for airline pilots, only between WS and UA ($P = 0.010$), and between WS and STF ($P < 0.01$), the differences were significant.

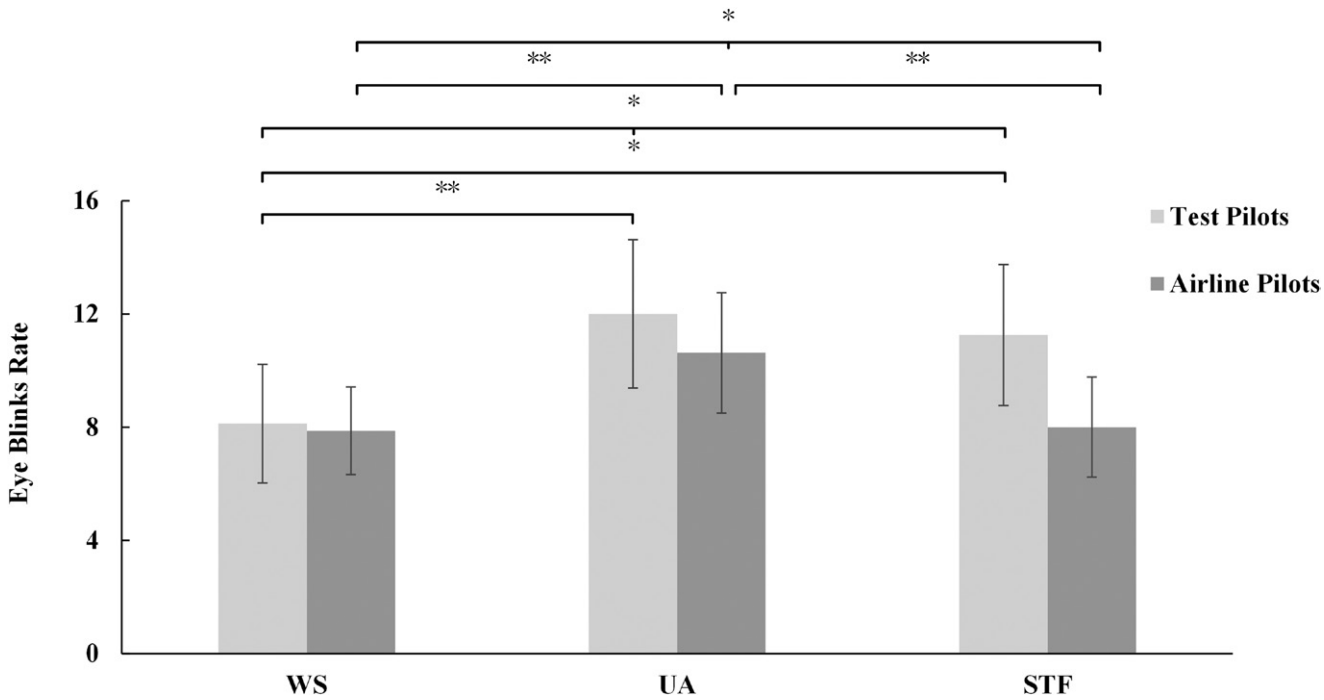

Fig. 1. The results of Eye blinks rate of test pilots and airline pilots in three flight tasks, which were Encountering Wind Shear after lifting off (WS), Unreliable Airspeed during taking off (UA) and Stabilizer Trim Failure (STF) (* $P < 0.05$, ** $P < 0.01$) . The error bars stand for the SD of eye blinks rate of the subjects either for test pilots or for test pilots.

Encountering Wind Shear After Lifting Off

In this scene, we were interested in reaction time to wind shear and pitch angle deviation during the climb. The reaction time was the interval from 'wind shear' flashing and voice warning appeared to the pilots pushing the throttle to the maximum position. The pitch angle deviation was equal to the difference between the pilot's average pitch angle and 18° during disengagement from wind shear. The mean reaction time of test pilots to wind shear was 3.96 s (SD = 0.72), and for airline pilots, the average reaction time was 4.05s (SD = 0.72). Comparing their reaction time revealed no significant difference [F (1, 14) = 0.06, $P = 0.811$]. Further, there was significant

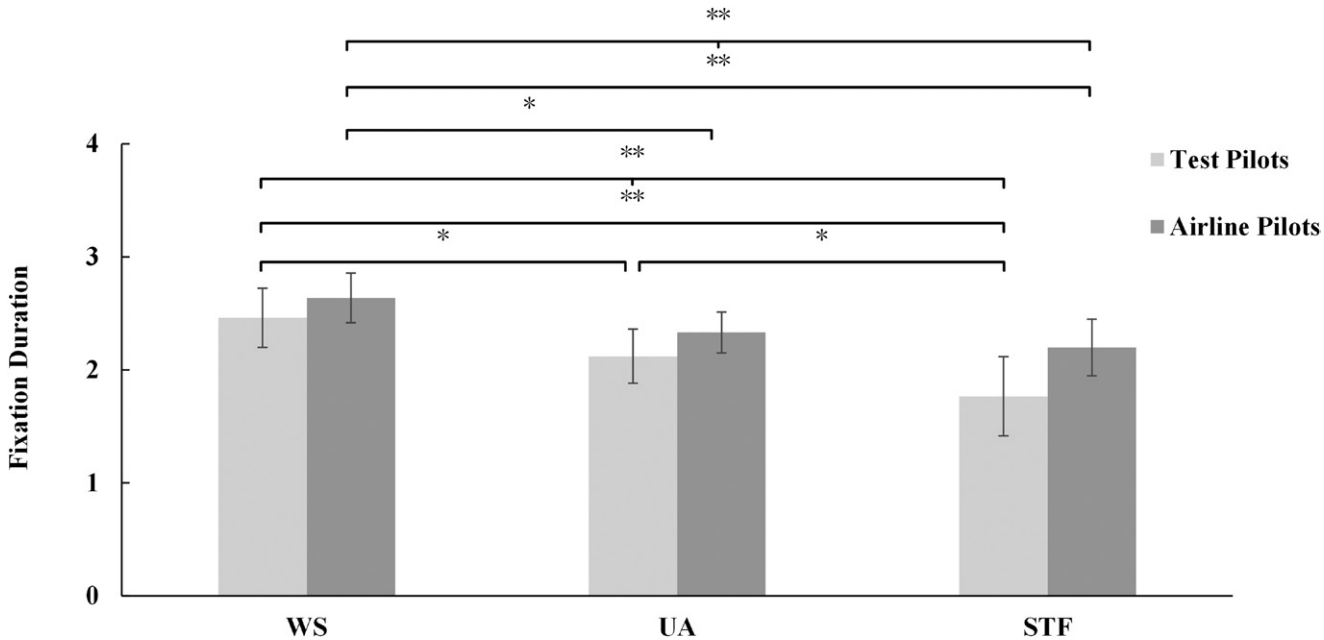

Fig. 2. The results of fixation duration of test pilots and airline pilots in three flight tasks, which were Encountering Wind Shear after lifting off (WS), Unreliable Airspeed during taking off (UA) and Stabilizer Trim Failure (STF) (* $P < 0.05$, ** $P < 0.01$) . The error bars stand for the SD of fixation duration of the subjects either for test pilots or for test pilots.

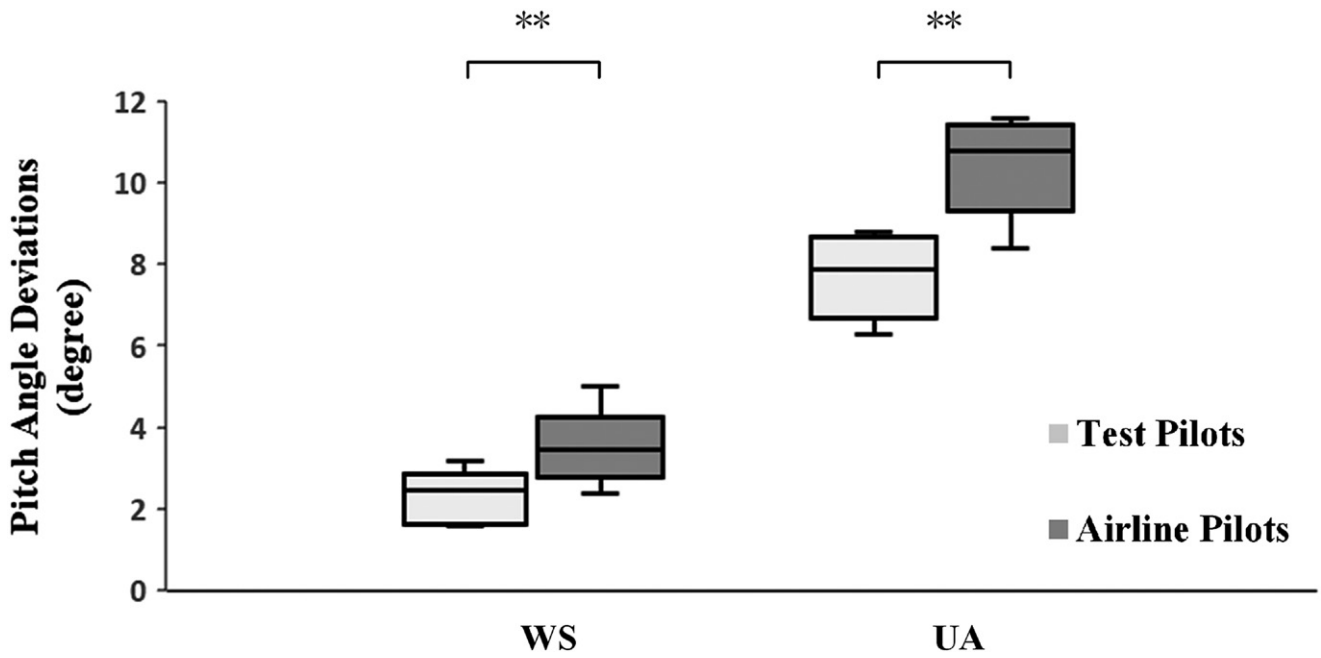

Fig. 3. Pitch angle deviation of test pilots and airline pilots in two flight tasks, which were Encountering Wind Shear after lifting off (WS), Unreliable Airspeed during taking off (UA) (** $P < 0.01$).

difference [F (1, 14) = 10.08, $P < 0.01$] of the average pitch angle deviation between the test pilots and airline pilots (test pilots: 2.3° ± 0.64; airline pilots: 3.6° ± 0.89).

Unreliable Airspeed During Taking Off

In this scenario, we also paid attention to the reaction time to the unexpected event, which was from the pitot blockage occurred to the pilots leveling the airplane, and the average pitch angle deviation during the climb. The mean reaction time of test pilots to unreliable airspeed was 23.38 s (SD = 6.46), and for airline pilots, the average reaction time was 42.63 s (SD = 6.89). The difference between them was significant [F (1, 14) = 33.269, $P < 0.01$]. Otherwise, the difference of average pitch angel deviation between two types of pilots was also significant [F (1, 14) = 23.353, $P < 0.01$], test pilots (M = 7.74, SD = 1.03) were more precise in manipulating than airline pilots (M = 10.40, SD = 1.17). The pitch angel deviations of two types of pilots in WS and UA are shown in **Fig. 3**.

Stabilizer Trim Failure

In this task, we focused on two indicators, the reaction time to warning 'STAB FAULT', which was the period from when the alert took place to when STAB TRIM was pressed, and the landing speed deviation, which was equal to the difference between actual landing speed and VRef Full +15kts. The mean reaction time of airline pilots (M = 4.86 s, SD = 0.58) was slightly shorter than test pilots (M = 5.54 s, SD = 0.77), however, the difference was insignificant [F (1, 14) = 3.927, $P = 0.068$]. Moreover, statistically different landing speed deviations was found (test pilots: 3.50 knots ± 1.60; airline pilots: 3.63 knots ± 1.92), but of no practical significance [F (1, 14) = 0.020, $P = 0.890$], as shown in **Fig. 4**.

DISCUSSION

In this study, three abnormal scenes were carried out in an A320 D-level flight simulator, one is where the aircraft was in an unexpected ambient environment (WS), and the other two were system failures (UA, STF). Considering the eye movement data, it seemed that the uncertainty of environmental change would give rise to more severe pressure and mental workload influence than system failure with minimum eye blink rate and maximum fixation duration in wind shear condition both for test pilots and airline pilots. This result is reasonable, according to findings of National Research Council, when encountering severe weather conditions, such as low altitude wind shear, the aircraft may deviate from the normal trajectory or even lose stability rapidly, which poses a great safety risk for flight, especially in take-off and landing phase.[4] Comparatively, the failure of a single system would not lead to disastrous consequences, as the important systems on the aircraft have redundant design.[1] Even for the failure or jamming of one control surface, pilots can still manipulate the aircraft through other controls.

This also explains why strong crosswind and natural icing test flights are the most challenging high-risk test subjects in the certification progress.

In the scenario of WS, pilots could recognize the unexpected event immediately based on warning information, and only needed to increase the pitch angle and maintain it at a constant degree until eliminating wind shear (2000 ft). The duration of the scene was relatively short, and the angle manipulating requirement was fixed. However, in the scenario of UA, the pilot was required to identify the failure on his own initiative and adjust the pitch angles at different flight levels until

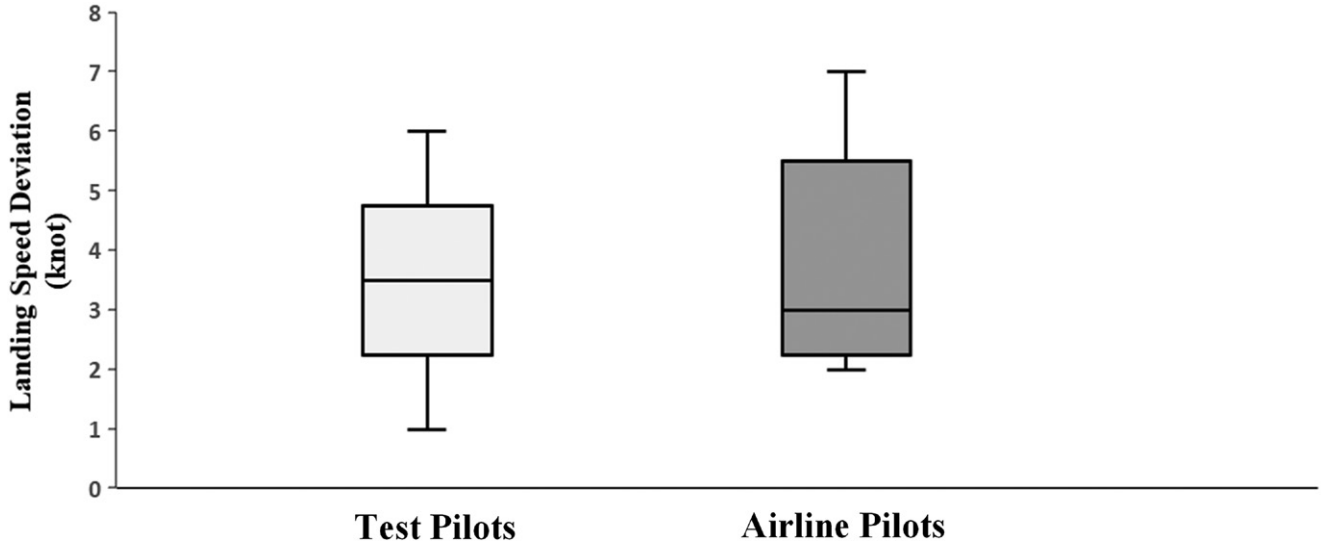

Fig. 4. Landing Speed deviation of test pilots and airline pilots in Stabilizer Trim Failure.

climbing to 20,000 ft. The operation was more complicated and took longer, resulting in a larger deviation of control accuracy. Specifically, when encountering an unexpected environment condition (WS), the test pilots performed significantly better than airline pilots in terms of aircraft manipulation. It is undeniable that all pilots who can serve as captains have undergone strict training and assessment and are capable of ensuring flight safety. However, since the daily work of test pilots is to be exposed to uncertain surroundings and medium or high-risk conditions, identifying potential inconspicuous risks is a rule-based behavior for them, while for ordinary pilots, it may still be in the knowledge-based level according to Rasmussen's human performance model.[19] Therefore, the disposal measures for some unexpected events, based on configurations of control flight elements (attitude and power), might have become the content of test pilot's long-term working memory.[22] This allows them to achieve more sophisticated and accurate operations according to the standard procedures, which not only can bring better safety margin, but also make the aircraft operate in an economical state. The indicators in the flight manual are the relatively optimal values calculated based on parameters such as aircraft weight and center of gravity. Such accurate control is particularly evident in the long-term operation requirements, i.e., manual angle control. Nevertheless, for both test pilots and airline pilots, the precise control requirements of single point could be well met, for instance, the landing speed. Orlady assumed as takeoff and landing phases are the most common scenes in flight training, qualified pilots have an intimate knowledge of the parameters that might affect safety at critical flight moment and could implement them at the optimal time.[16]

Otherwise, reaction time was also selected as pilot's performance indicator in this study, as one hallmark of expertise is the speed at which experts work, as Masunaga and Horn suggested.[13] In two scenarios with warnings (WS, STF), the differences in reaction time of test pilots and airline pilots were insignificant. In detail, in wind shear condition, the average reaction time was shortest both for two types of pilots, and test pilots was significantly faster than that of airline pilots. Surprisingly, when stabilizer trim fault occurred, the test pilots' reaction was slightly slower. The phenomenon might be a result of any of the following reasons. Firstly, in case of warning, a corresponding alert tone and a red highlight information would appear in flight deck to ensure the immediate pilot's awareness and immediate action.[18] Therefore, all the well-trained pilots were able to respond in time in scenarios with alarm prompts. Secondly, when encountering wind shear, a flashing light in the primary flight display and speech warning would emerge, which could grab the pilot's attention more quickly than the warning only display in crew alerting system with the unified auditory indication. Single tones provide no information as such, so it is not surprising that a speech warning system would out-perform such meager nonverbal signals.[6] Smith et al. also found speech warnings provided an advantage in reaction time and response accuracy over auditory icon warnings.[21] Thus, speech warning should be used in the most common emergency situation, such as stall, because it requires very little cognitive processing and has the ability to alert and to inform the nature of the hazard.[15] Thirdly, although test pilots were slower in stabilizer trim fault condition, their reaction time was in an acceptable range and still could control the aircraft appropriately. Moreover, the trim failure was a kind of appearance, which would be triggered by a variety of reasons. The test pilot might spend more time exploring the root fault to enhance the situation awareness, rather than simply follow the flight manual.

Conversely, without alarm, pilots need to identify the differences of numerical information on displays and determine whether the flight parameters were reliable by themselves, resulting in a sharp increase of the reaction time in scenario UA. Stanton and Edworthy found an auditory warning would lead to a quicker response than visual stimulus.[23] However, the performance of test pilots was significantly better than that of ordinary pilots, and they could detect the occurrence of

unreliable airspeed in a relatively short time. In real flying, the airline pilots might perform even less efficiently, since test pilots encounter sudden changes, unusual attitudes, and aircraft performance extremes more often in research and development test flight or certification test flight in new or modified aircrafts. The states and configurations of such aircrafts are usually not as stable as that of aircrafts normally operated by airlines. Furthermore, test pilots fly close to the safety boundaries more frequently to test and validate the performance and characteristics of the aircraft in test flight. Some flight test scenarios with rare system faults or with rigorous surroundings might never be met by airline pilots.[25] This kind of boundary detection requires test pilots to be more circumspect and sensitive to changes in aircraft status and enables them to respond more quickly to unannounced faults, thus effectively improving the safety level of test flight.

By comparing the physiological reactions and performance of test pilots and airline pilots when facing the unexpected events in this research, there are three aspects would be enhanced in airline pilots training. First, although a great quantity of automated equipment could be used, the importance of manual flight should still be emphasized, which allows pilots to precisely control the aircraft without the help of automation system for a long period. Secondly, increasing the training of flight in unexpected ambient conditions, especially during takeoff and landing phase, because changes in the environment are more likely to cause pilots to startle, and such critical flight phases require them to respond more timely. Last, but not least, improving the reaction to the unannounced fault status, would allow pilots to cope with deviations more calmly and reduce safety risks.

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Spaceflight Maximum Allowable Concentrations for Ethyl Acetate

E. Spencer Williams; Valerie E. Ryder

INTRODUCTION: Ethyl acetate is a simple organic compound that occurs naturally and is used industrially as a solvent. It has been detected in the ISS atmosphere and is known to off-gas from building materials. As NASA astronauts have been and will be exposed to ethyl acetate during space missions, Spaceflight Maximum Allowable Concentrations (SMACs) were developed following an extensive review of the available literature.

METHODS: Toxicological data relevant to SMAC development was collected from electronic databases using principles of systematic review, and from previous assessments and reviews of ethyl acetate.

RESULTS: From an initial pool of over 35,000 studies, 10 were identified as studies appropriate to support SMAC development. The toxicological properties of ethyl acetate are relatively straightforward. Ethyl acetate is rapidly absorbed and converted by carboxyesterases to ethanol. At concentrations on the order of 400 ppm for 4–8 h, most volunteers experienced mild irritation but no lasting effects. In subchronic animal studies, mild sedative effects and changes in body weight and weight gain were observed at 750 ppm and above.

DISCUSSION: Numerous studies were identified to support the development of both short- and long-duration SMACs. No chronic studies were available, but the high quality of the subchronic studies and the short half-life of ethyl acetate support extrapolation to longer durations.

KEYWORDS: SMAC, spaceflight, International Space Station, astronaut, spaceflight environment, air quality, ethyl acetate, volatile organic compounds, offgassing.

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Ethyl acetate is a simple organic compound that occurs naturally in fruit and as a byproduct of fermentation (hence its presence in wine and other spirits).[35,40] It is "generally regarded as safe" (GRAS) by the United States Food and Drug Administration and is used as an approved flavoring agent in food and pharmaceuticals. Industrially, it is used as a solvent and is manufactured on a tremendous scale. Ethyl acetate is commonly used to isolate hydrophobic fractions of natural products for use in commercial and medicinal applications.[30,41]

Occupational exposure to ethyl acetate occurs in settings where lacquers, inks, adhesives, coatings, or solvents are used.[51] A number of studies have examined potential exposures in nail salons, along with acetone, acrylates, and other volatile organic compounds.[28] Numerous safety values are available for ethyl acetate (**Table I**).

Ethyl acetate is rarely flown as part of a payload to ISS, but it is occasionally detected in ISS air by the Air Quality Monitors (AQMs) and in routine sampling through mini grab sample containers (mGSCs). Ethyl acetate off-gasses from building materials[49] and has occasionally been detected at low levels in off-gas testing for NASA vehicles and equipment.[8]

METHODS

A strategy for gathering scientific data using principles of systematic review was designed according to the guidelines provided by the Office of Health Assessment and Translation and similar to that employed by the Agency for Toxic

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Table I. Existing Safety Limits for Ethyl Acetate.

ORGANIZATION	VALUE	PPM	mg · m^{-3}	DATE
EPA	*P*-RfC$_{subchronic}$	0.2	0.7	2013
	p-RfC$_{chronic}$	0.02	0.07	
OSHA	PEL	400	1470	
	STEL			
NIOSH	REL	400	1470	1992
ACGIH	TLV	400	1470	2001
CDC	IDLH	2000	7200	
SCOEL	8h TWA	200	730	2008
	STEL	400	1470	
MAK		400	1440	1958

Substances and Disease Registry in their toxicological profile for antimony.[2,39] A PECOT (population, exposure, comparators, outcomes, timescales) table was developed to clarify the criteria for inclusion in the review (**Table II**). Briefly, the systematic review sought to identify reliable and robust research studies in humans and laboratory animals which examine numerous toxicological endpoints following exposure to ethyl acetate and which identify explicit dose descriptors (e.g., NOAEC) that may serve as points of departure for SMAC development.

Table II. PECOT Parameters for Systematic Review for Ethyl Acetate Toxicity Data.

Populations	Humans
	Laboratory animals
Exposures	Inhalation
	Ingestion
	Dermal
	Other
Comparators	Controls
	Subjects exposed to lower doses
Outcomes	Eye irritation
	Skin irritation
	Skin sensitization
	Respiratory sensitization
	Systemic effects
	Respiratory
	Cardiovascular
	Gastrointestinal
	Hematological
	Musculoskeletal
	Hepatic
	Renal
	Endocrine
	Dermal
	Ocular
	Body weight
	Metabolic
	Other effects
	Immunological effects
	Neurological effects
	Reproductive effects
	Developmental effects*
	Cancer
Timescales	Acute
	Subacute
	Subchronic
	Chronic
	Other

* Developmental effects are not considered in setting SMACs, as they are not relevant to spaceflight exposure scenarios. However, data from these studies can be informative for other endpoints.

The final search term was: "ethyl acetate" OR "Acetic acid ethyl ester" OR "Acetic acid, ethyl ester" OR "Acetic ether" OR "Acetidin" OR "Acetoxyethane" OR "Ethyl ethanoate" OR "Ethyl ester" OR "Ethyl acetic ester" OR "141-78-6". Gathering of potential data sources was performed in October 2018. An additional search was conducted in August 2021 to verify that no additional studies had been published after the earlier review date. During the process of systematic literature review, numerous errors in dating of articles were noted in the results from the Toxline Database. Also, numerous references from HERO were not gathered in the search. Further exploration indicated that searching the HERO database via its web interface did not gather all resources even with the sole search term "ethyl acetate," though it appeared in the title of numerous resources cited in other documents and found on HERO through other search strategies.

Careful curation of the data sources was required, as several sources were duplicated by different authors; the root cause of this is the provenance of the documents through regulatory submissions. For example, studies conducted by Union Carbide[9] and Haskell Laboratories[11,12,14] were also identified as emanating from the trade association representatives who submitted the documents for regulatory review (i.e., CM Price and

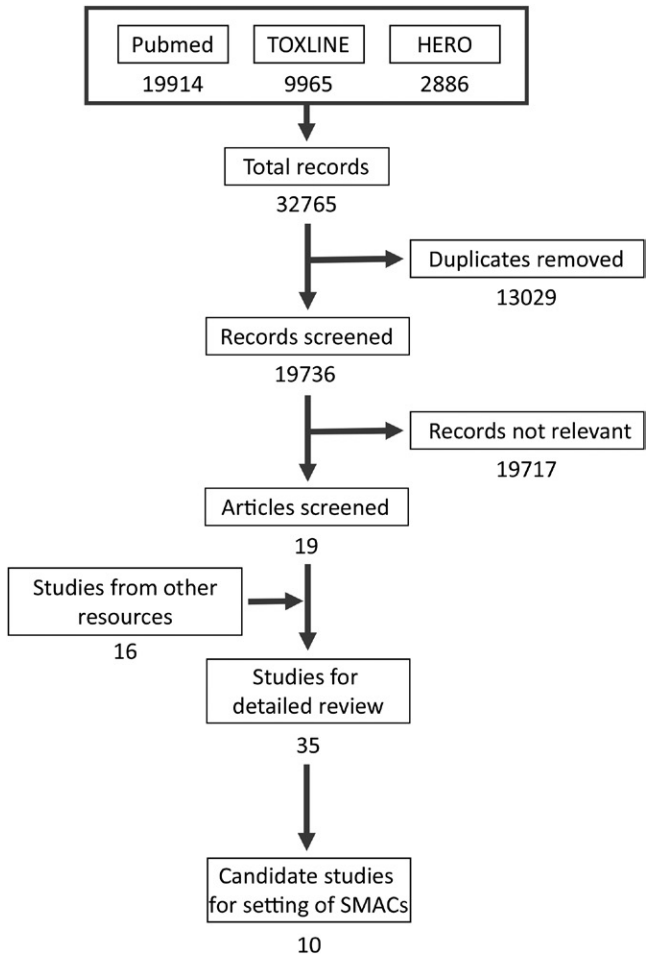

Fig. 1. Study selection process and metrics for systematic review of ethyl acetate toxicology.

LA Spurlock). From the electronic resources, 32,765 records were gathered. The use of ethyl acetate to extract natural product mixtures is responsible for the large number of initial resources identified by database searches. Screening reduced the original data set to 19 relevant articles and reports (**Fig. 1**).

To ensure our review was comprehensive, we scrutinized prior assessments of ethyl acetate which included a PPRTV,[21] a data summary generated by EPA's Integrated Risk Information System,[22] two occupational safety values from the EU,[23,24] a Cosmetic Ingredient Review (CIR),[29] and a SIDS Initial Assessment Report.[40] From review of summary sources, 16 studies were added for a total of 35 studies for detailed review. Several of these are overlapping or redundant, as numerous reports were generated from the same studies (**Table III**), and a subset of 10 studies were ultimately used for setting of SMACs. Each study was reviewed for Risk-of-Bias using the IRIS framework for assessing data quality. Of the 10 studies selected, only 1 (Nelson[36]) was regarded as "low confidence" based on a lack of available information for study design and interpretation. ACGIH, however, viewed this study as sufficiently robust to set their threshold limit value.[1,36] All other studies were rated as medium or high confidence.

RESULTS

Toxicokinetics

Ethyl acetate is rapidly absorbed during inhalation exposures in both animals and human volunteers.[37,50] The available data demonstrate ethyl acetate is also rapidly eliminated via enzymatic and nonenzymatic hydrolysis to ethanol and acetic acid.[16,29] Following ingestion exposures, the half-life of ethyl acetate in blood is on the order of 35 s and attributable primarily to rapid metabolism by carboxyesterases in organs.[18,26] In rats given intraperitoneal injections of ethyl acetate, high concentrations of ethanol were detected within 5 min, and ethyl acetate became undetectable after 20 min.[26] Ethanol predominated in the tissues of a 39-yr-old worker who died from acute ethyl acetate intoxication.[15]

In another study, rats were exposed to 500–10,000 ppm ethyl acetate via endotracheal tube. Accumulation of ethanol in rats only occurred in exposures exceeding 2000 ppm ethyl acetate.[23,26] At very high concentrations (e.g., 10,000 ppm), ethanol accumulates rapidly and causes respiratory depression. The European Commission's Scientific Committee on Occupational Exposure Limits (SCOEL) judged that, due to its

Table III. Summary of Relevant Toxicological Studies on Ethyl Acetate.

SPECIES AND NUMBER	EXPOSURE DURATION	TARGET EXPOSURE LEVELS (PPM)	RESULTS	DOSE DESCRIPTOR	LEVEL	REFERENCE
Human volunteers (4M, 4F)	2h × 6	15 ppm	No changes were observed in measures of eye or respiratory irritation.	NOAEC	15 ppm	20
Human volunteers (*N* = 10)	3-5m	200, 400 ppm	Subjects described 200 ppm as "objectionable" due to strong odor.	NOAEC LOAEC	200 ppm 400 ppm	36
Human volunteers (*N* = 16)	4 or 8 h	400 ppm	Increased reports of moderate irritation were reported among volunteers relative to controls.	LOAEC	400 ppm	45
Human volunteers (*N* = 32)		400 ppm	Increased reports of "annoyance" were reported among volunteers relative to controls.	LOAEC	400 ppm	46
Human volunteers (*N* = 24)	4h	400 ppm	Subjective reports of olfactory symptoms were markedly increased at 400 ppm.	LOAEC	400 ppm	32
Human volunteers (*N* = 4 and 6)	4h	200, 400 ppm	Irritation was not observed at 200 ppm, but mild irritation in eyes, nose, and throat were reported at 400 ppm in 2 of 6 subjects.	NOAEC LOAEC	200 ppm 400 ppm	34
CD Rat (14/sex/treatment)	6h	0, 600, 3000, 6000 ppm	No overt clinical signs were observed as a result of treatment. Dose-dependent changes in body weight were observed at all dose levels.	NOEL (neurotoxicity)	600 ppm	9
CFW mice (*N* = 8, male)	20m	0, 250, 500, 1000, 2000 ppm	Significant decreases in locomotor activity were observed in mice exposed to 2000 ppm but all were reversible after exposure concluded.	NOAEL (neurotoxicity)	1000 ppm	9
Rat	6h/day, 5d/week, 2 wk (60 h)	0, 1500, 3000, 6000 ppm	Decreased body weight and weight gains were noted in all exposure groups (only among females).	LOAEC	1500 ppm	9
Crl: CD BR rat	10 h over 2 wk	1500 ppm	Decreased body weight and weight gain were observed.	LOAEC	1500 ppm	11,12,13,14
Crl:CD BR rat (*N* = 40)	6 h/day, 5d/week, 89 d (385.5 h)	0, 350, 750, 1500 ppm	Microscopic lesions in olfactory tissues and minor reductions in weight gain in male rats were noted in 8 of 20 animals at 350 ppm.	NOEC*	350 ppm	11,12,13,14

*The study documents refer to this dose level as a LOAEC for body weight loss and nasal lesions in rats. EPA has determined that this dose level is a NOAEC as the body weight changes are not significant and the microscopic nasal lesions in rats are not relevant to human receptors.

rapid hydrolysis, ethyl acetate is unlikely to cause systemic effects and that the critical acute effect for ethyl acetate is irritation of the upper respiratory tract.[21]

According to Fleury and Wirth,[25] acute exposures to rabbits at 20,500 ppm (75,000 mg · m^{-3}) led to a reduction in blood pH of only 0.07; this indicates ethyl acetate exposures at concentrations that protect against irritation would not lead to acidosis.[29]

Crowell et al.[16] developed a PBPK model that incorporated the metabolic series approach to account for the sequential metabolism of ethyl acetate to ethanol and through subsequent steps. The model was populated using published data from in vitro and in vivo studies supplemented by findings from IV infusions of ethyl acetate in rats. Rats were given either an IV bolus of 10 or 100 mg · kg^{-1} ethyl acetate, or a 15-min infusion of 10 or 50 mg · kg^{-1}. Data from the 15-min infusion demonstrates a rapid decrease in blood levels of ethyl acetate while ethanol rises during the infusion and begins a slow decrease after the exposure ends. Similar conclusions can be drawn from the bolus dose. The predicted values are in very good agreement with data from the infusion studies. Additionally, the evidence demonstrates the elimination pathways for ethyl acetate (especially carboxyesterases) are not saturated at 100 mg · kg^{-1} as previously demonstrated.[16,18]

Toxicity

The most important toxicological outcomes following exposure to ethyl acetate vapors include irritation and neurological decrements. Acute exposures to higher concentrations can cause nausea and vomiting, and CNS depression. The odor threshold for ethyl acetate ranges from 3.6 – 245 ppm (24-900 mg · m^{-3}).[21]

Irritation

Several studies conducted in human volunteers have demonstrated ethyl acetate vapor can be irritating at high concentrations (> 400 ppm or 1470 mg · m^{-3}) and that 200 ppm (730 mg · m^{-3}) ethyl acetate carries an "objectionably strong" odor for unacclimated workers.[1,43] In a group of 10 volunteers exposed to ethyl acetate for 3–5 min, most reported 100 ppm (360 mg · m^{-3}) would be tolerable for an 8 h exposure and 200 ppm was not irritating but had an intense odor.[36] McCallum et al. reported irritation effects were not observed at 200 ppm for 4 h (N = 5), but were observed in two of six individuals at 400 ppm.[34] Kleinbeck et al. subjected 23 volunteers to ethyl acetate at 2 ppm, 400 ppm, and variable levels beginning at 5 ppm and peaking at 800 ppm (2900 mg · m^{-3}) four times during the exposure period of 4 h.[32] Half of respondents described the severity of olfactory symptoms as "rather much," "considerably," or "very, very much." Despite this result, the authors describe 800 ppm as "minimally irritating" and 400 ppm as "bearable during long-term exposure." Similarly, Seeber et al. exposed volunteers to 400 ppm ethyl acetate for 4–8 h and determined some irritation and annoyance occurs at that level.[45,46] Dwivedi et al. used 15 ppm ethyl acetate to mask the odor of acrolein during an irritation test for that substance, and no effects were observed from exposure to ethyl acetate at that level for 6 episodes of 2 h among 8 volunteers.[20]

Instillation of 1 drop of ethyl acetate into a rabbit eye led to reddening and slight conjunctival swelling that regressed after 1–2 d. In cats, concentrations higher than 4200 ppm (15,100 mg · m^{-3}) caused closed eyes and lacrimation.[25] Direct application of ethyl acetate to skin leads to defatting and damage to the strateum cornum.[29]

Acute Effects

The LC50 for ethyl acetate for rats is on the order of 55,500 ppm (200 g · m^{-3}) in rats and 12,500 ppm (45 g · m^{-3}) in mice.[5,44] Ethyl acetate was fatal in cats after a 15-min exposure to 43,000 ppm (155,000 mg · m^{-3}), while 9000 ppm (32,000 mg · m^{-3}) caused irritation and labored breathing. Exposure to 20,000 ppm for 45 min caused deep narcosis.[52]

Several summary sources reported the findings of Smyth and Smyth, in which three guinea pigs were exposed to ethyl acetate at 290 ppm (1030 mg · m^{-3}) in "gassing jars."[47] ACGIH noted the animals withstood ethyl acetate concentrations of 2000 ppm (7200 mg · m^{-3}) for 65 exposures (4-h each) without effects on body weights or clinical blood parameters.[1] The investigators observed anemia secondary to leukocytosis and liver damage in rabbits exposed to 4450 ppm (16,000 mg · m^{-3}) ethyl acetate.[1,47,52]

Bowen and Balster assessed the acute neurobehavioral effects of ethyl acetate on mice (N = 8) following a single 20-min inhalation exposure at 0, 500, 1000, or 2000 ppm (0, 1800, 3600, 7200 mg/m^3).[7] At the highest concentrations, ethyl acetate caused decreased locomotor activity and other behavioral changes. Spasmodic movements were observed at all concentrations tested, but these were not recorded in a robust way and thus cannot be evaluated. The animals recovered within minutes after removal from the exposure chamber.

DuPont de Nemours conducted a study in dogs to determine the comparative toxicity of three acetic acid esters: methyl acetate, ethyl acetate, and N-butyl acetate.[19] The exposure was to levels estimated to be approximately half of the dose required to induce narcosis; for ethyl acetate, this was 22 mg · L^{-1} (equivalent to 22,000 mg · m^{-3}, or 6100 ppm). The authors note the actual concentrations may vary as much as 10%. Two dogs per concentration were exposed for 40 min/d, twice a week, for 4 wk (total exposure time: 5.3 h). The measures used were generally subjective. Ethyl acetate was noted to elicit "excitement" in the dogs posttreatment, but not as potently as methyl acetate did. The symptoms were barking, whining, pawing, and walking with a staggering gate. One dog was noted to have tremor. Ethyl acetate induced vomiting, and moderately increased the rate of respiration (not quantified). Exposure to ethyl acetate was also said to induce "a trend toward circulatory abnormality" and a fall in venous blood pressure. Other effects included a rise in rectal temperature, irritation (salivation, lacrimation), and prolonged "unsteadiness." Given the nature of the experiments, this report is not informative in the setting of SMACs, but useful in terms of high-exposure effects.

Subacute Effects

Burleigh-Flayer et al. exposed groups of rats (10 males and 5 females per group) to ethyl acetate by whole-body inhalation at 1500, 3000, and 6000 ppm (5400, 11,000, and 22,000 mg · m^{-3}) for 6 h/d, 5 d/wk for 2 wk (i.e., a total of 60 h over 10 d).[9] Neurological symptoms were assessed via a functional observational battery (FOB) and motor activity testing before and after exposure. Body weights, clinical symptoms, and food and water consumption were reported through the exposure period. As reported by EPA, neurological symptoms were observed at 3000 and 6000 ppm, including decreased startle reflex, abnormal eye responses, and hypoactivity. Changes in body weight-corrected brain and ovary weights were noted in female rats at the upper concentrations. Concentration-dependent decreases in body weight and food consumption were also observed. A LOAEC of 1500 ppm was identified for this study, based on decreased food consumption. Human equivalent concentrations (HECs) were calculated using standard methodology but without the benefit of physiologically based pharmacokinetic modeling.

Subchronic Effects

The strongest body of evidence on ethyl acetate toxicity comes from a series of subchronic tests conducted at the Haskell Laboratory for Toxicology and Industrial Medicine. The investigators exposed Sprague-Dawley rats via chamber (i.e., inhalation) to 0, 350, 750, and 1500 ppm (0, 1300, 2700, and 5400 mg · m^{-3}) for 6 h/d, 5 d/wk for 13 wk (i.e., a total of 390 h over 65 d)[13] and examined neurotoxicological[12] and operant behavioral outcomes,[11] as well as olfactory pathology.[14] The top dose level was based on the subacute study conducted by Burleigh-Flayer et al.[9]

In the neurobehavioral study, 12–18 animals of each sex at each dose level were subjected to an FOB and motor activity assessment on nonexposure days or after a 4-wk recovery period. Diminished startle responses were observed in the 750 and 1500 ppm exposure groups. The investigators determined the decrement was a threshold effect related to frank narcosis seen at 5000–12,000 ppm in other studies. Changes in grip strength were observed in female rats at 350 and 1500 ppm but were determined not to be related to ethyl acetate treatment. No sensory or motor anomalies were identified via the FOB in this study. Neuropathological evaluation did not reveal any structural abnormalities.

No compound-related reductions in organ weight were observed, though spleen weight was lower and adrenal weight was higher in the highest treatment group. These changes were described as secondary to lower body weight. No compound-related effects were observed during gross pathology.[14] Microscopic pathological analysis was conducted on the neurological system, testes, and nasal mucosa. At the lowest dose level (350 ppm), microscopic lesions were observed in olfactory mucosa in 8 of 20 animals and were graded as minimal. These lesions were observed in 100% of animals at the higher dose levels and graded as "minimal to moderate" for the 750 ppm group and "minimal to severe" for the 1500 ppm group. As a result, no NOAEC could be established. 350 ppm might be considered as a LOAEC for rats in this experiment, on that basis. Lesions of this type are common in rats exposed to acetate esters due to tissue-specific liberation of acetic acid.[40] For that reason, and due to physiological and anatomical differences in nasal structures, their relevance to human health is uncertain.[10,27,40]

Concentration-dependent decreases in body weights were observed in both sexes, accompanied by decreases in food consumption. The EPA analyzed the changes in body weights and determined the reductions in body weight at the lowest dose level (350 ppm) was not physiologically significant. Thus, the NOAEC for ethyl acetate was determined to be 350 ppm, and a LOAEC at 750 ppm based on decreased body weights, food consumption, and startle responses. This study was chosen as the principal study for p-RfC by the EPA.[23] As noted by the EPA, data reporting was not sufficient to allow for benchmark dose modeling. As with the shorter-term study, HEC for each dose level were calculated using duration adjustment to a 98-d exposure period as no PBPK model existed at the time.

Crowell et al. applied their PBPK model to the data generated by Christoph et al. to generate human equivalent concentrations (HECs).[16] The model indicates that a dose level of 350 ppm in the study is commensurate with an HEC of 495 ppm for an 8 h/d, 5 d/wk (i.e., occupational) exposure and a continuous HEC of 119 ppm (based on blood levels of ethyl acetate). The authors describe the 350 ppm dose level as a LOAEC due to body weight losses, though EPA notes the "small decreases in body-weight gain and food efficiency at [350 ppm] are not considered biologically significant" and refers to this exposure level as a NOAEC.[23] Though the model is not validated with human toxicokinetic data for ethyl acetate, the ethanol portion of the model is considered robust given the wealth of data for that substance. However, the model did overpredict blood ethanol concentrations arising from whole-body ethyl acetate exposures in rats. The authors postulate this is due to lung-specific metabolism of ethyl acetate upon inhalation, whereas the PBPK model was calibrated using intravenous bolus doses. The HEC from this study will be considered as a candidate for the setting of SMACs with the addition of appropriate uncertainty factors. Given the calculated HEC for continuous exposure is threefold lower than the NOAEC, it is expected to produce similar SMAC values as use of a standard uncertainty factor of 3 for interspecies differences in toxicokinetics/toxicodynamics.

No controlled chronic inhalation studies are available for ethyl acetate. Limited data are available from numerous occupational cohorts exposed to ethyl acetate over longer periods, though generally other solvents are also present. ACGIH notes findings described by Patty in which workers were regularly exposed to 375–1500 ppm (1350-5400 mg · m^{-3}) for several months but showed "no unusual signs or symptoms"[1]. The Dutch Expert Committee for Occupational Standards reported workers who were exposed to ethyl acetate at concentrations ranging from 4200–14,000 ppm for 2 wk to several years suffered numerous symptoms of ongoing eye irritation

(lacrimation, edema on eyelids, conjunctival irritation).[29] Occupational studies of workers in paint spraying and a shoe factory are also discussed, but their confounding exposures to unspecified solvents and tolene/xylene make it difficult to determine whether any effects can be attributed to ethyl acetate.[29] As ethyl acetate is rapidly metabolized and eliminated, it is likely the duration of exposure is not a critical determinant of long-term toxicity (especially at lower concentrations).[29,42]

Mutagenicity/Genotoxicity

Ethyl acetate produces aneuploidy in yeast assays but does not appear mutagenic or genotoxic in the Ames, sister chromatid exchange, or chromosomal aberration assays.[4,31,53] When administered to mice interperitoneally (3 doses/week for 8 wk), no increase in tumors was noted, nor did one-time dermal application of ethyl acetate to the skin of mice produce any increase in papilloma incidence.[33,48] Basler also dosed hamsters with ethyl acetate via intraperitoneal injection (473 mg · kg^{-1}), and no increase in micronuclei was observed.[4] No chronic carcinogenicity studies are available for ingestion or inhalation exposures.

Existing Safety Values for Ethyl Acetate

ACGIH has set a Threshold Limit Value of 400 ppm (8-h time weighted average, TWA), based on Nelson et al. and includes the expectation that some workers may experience mild irritation.[1,36] This value is consistent with those endorsed by OSHA and NIOSH in the United States, and a maximum workplace concentration (MAK) set by Germany in 1958. The SCOEL re-evaluated their safety values on ethyl acetate in 2008 and promulgated an 8-h TWA value of 200 ppm and a Short-Term Exposure Limit (STEL; 15 min) of 400 ppm.[21] This value was predicated on the same data as ACGIH and supplemented by information from the subacute and subchronic studies in rats.

EPA's subchronic p-RfC of 0.2 ppm (0.7 mg · m^{-3}) was set based on the NOAEC of 350 ppm from subchronic studies in rats.[13] This level was adjusted to a HEC of 209 mg · m^{-3}, which was divided by 3000 to account for interspecies differences in toxicodynamics (3), interindividual differences in susceptibility (10), and lack of an acceptable two-generation reproductive or developmental toxicity study (10). The chronic p-RfC was divided by an additional uncertainty factor of 10 to address lifetime exposure from a subchronic study, rendering a final value of 0.02 ppm (0.07 mg · m^{-3}). As SMACs are set for healthy adults, they generally do not account for sensitive subpopulations as terrestrial safety values do. Also, given that SMACs are set for less-than-lifetime exposure durations in persons who are not pregnant (or likely to become pregnant), developmental toxicity is not considered.

Summary of Development of Updated SMACs

Spaceflight factors. When setting SMAC values, NASA occasionally includes an additional uncertainty/safety factor to protect against toxicological outcomes that may be compounded by exposure to the spaceflight environment. For example, hypercalcemia and hypercalcuria have been observed for all crew members as a result of weightlessness, and thus any chemical exposures impacting the remodeling of bone or modulation in circulating calcium levels might require an additional safety factor to reduce the hazard. However, the toxicological endpoints of interest for ethyl acetate (irritation in humans, body weight losses and slight neurobehavioral changes in animals) do not justify the use of an additional factor in setting SMACs.

EFSA's review of ethyl acetate mentions a study that suggests ethyl acetate may cause immunosuppression; however, this study involves an ethyl acetate extraction of latex from a plant in the Euphorbiacae family.[3,5] Administration of this extract caused reductions in T-cell and neutrophil counts. Given the wealth of evidence that humans experience altered immune responses in spaceflight, such a finding would be relevant to the setting of a SMAC. Unfortunately, given the ambiguous nature of the test substance, it cannot be determined whether ethyl acetate is responsible for those reductions. Leukocytosis was noted in rabbits exposed to 4450 ppm ethyl acetate in a prior study, but no such observations were made in animals exposed to lower concentrations.[47]

1-h and 24-h SMACs. Short duration SMACs (1-h and 24-h) apply to accidental releases or other emergency scenarios on a spacecraft, and as such the values are set to permit minor, reversible effects (such as mild irritation).

Data from ethyl acetate exposures in human volunteers suggests that 400 ppm (over 4 or 8 h) is mildly irritating.[32,34,45,46] These observations are the basis for ACGIH's TLV of 400 ppm (1440 mg · m^{-3}) with the notation that mild irritation may be expected in workers who are unaccustomed to ethyl acetate exposure.[1] Further, ACGIH relayed observations from Patty's Toxicology that "workers exposed regularly at concentrations from 375 to 1500 ppm for several months showed no unusual signs or symptoms"[1]. Therefore, the 1-h SMAC is set at 400 ppm. The available studies in human volunteers extend no longer than 8 h. Multiple studies indicate that 200 ppm is not irritating in 4- or 8-h studies, but many respondents listed it as having an objectionably strong odor. Thus, the 24-h SMAC is also set at 400 ppm (**Table IV**). This level may be associated with minor, reversible irritation and odor complaints but is consistent with SMACs for off-nominal scenarios.

7-d SMAC. Two studies are available to support a 7-d SMAC value: Burleigh Flayer et al.,[9] and Christoph et al.[13] The total exposure period for rats in the study conducted by Burleigh Flayer is 60 h, while the subchronic studies conducted by Christoph et al. exposed rats to ethyl acetate for 390 h (compared to 168 h in a 7-d period).[13] Further, the study conducted by Burleigh Flayer identified 1500 ppm as a LOAEC (based on decreased food consumption) while Christoph identified a NOEC of 350 ppm (decreases in body weight and food efficiency). The application of the 350 ppm NOAEC from Christoph divided by an interspecies uncertainty factor of 3 (with no adjustment for exposure duration) yields a 7-d SMAC value of 117 ppm (Table IV). Additionally, the direct application of the adjusted NOAEC for continuous exposures in humans posited by Crowell et al. suggests a 7-d SMAC of 119 ppm.[16] Although this is expected to

TABLE IV. Spaceflight Maximum Allowable Concentrations for Ethyl Acetate.

ENDPOINT	EXPOSURE CONCENTRATION (PPM)	SPECIES	UNCERTAINTY FACTORS					SPACEFLIGHT MAXIMUM ACCEPTABLE CONCENTRATIONS (PPM)						REFERENCE
			NOAEL	DURATION	SPECIES	SPACEFLIGHT	DATABASE	1h	24h	7d	30d	180d	1000d	
LOAEL irritation, 8h	400	Human	1	1	1	1	1	**400**	NA	–	–	–	–	32,34,45,46
LOAEL irritation, 8h	400	Human	1	1	1	1	1	NA	**400**	–	–	–	–	32,34,45,46
NOAEC body weight, 90d*	350	Rat	1	NA	3	1	1	NA	–	**117**	–	–	–	11,12,13,14
NOAEC body weight, 90d*	350	Rat	1	NA	3	1	1	NA	–	–	**117**	–	–	11,12,13,14
NOAEC body weight, 90d*	350	Rat	1	NA	3	1	1	–	–	–	–	**117**	–	11,12,13,14
NOAEC body weight, 90d*	350	Rat	1	NA	3	1	3	–	–	–	–	–	**39**	11,12,13,14

*The study documents refer to this dose level as a LOAEC for body weight loss and nasal lesions in rats. EPA has determined that this dose level is a NOAEC as the body weight changes are not significant and the microscopic nasal lesions in rats are not relevant to human receptors.

protect against both irritation and neurological effects, it is within the reported range of odor thresholds and may present a habitability concern even if not directly toxic.

30-d and 180-d SMACs. As ethyl acetate is rapidly metabolized and doesn't accumulate, the degree of toxicity is a function of exposure dose rather than duration. Irritation as a toxicological endpoint, resulting from exposure to substances with brief half-lives, is regarded as being concentration-dependent and not dependent on duration of exposure.[6,17,42] As a result, no duration extrapolation need be applied to determine SMAC levels for 30- or 180-d. Thus, the value of 117 ppm derived as described above will also serve for these values.

Development of Extended-Duration (1000-d) SMAC

Little data exists to support the development of a comparison value for 1000 d. Again, the toxicokinetic data appears to support the adoption of the 180-d SMAC for the 1000-d SMAC, as ethyl acetate is rapidly converted to ethanol, and the ethanol doesn't accumulate in laboratory animals until the exposure level exceeds 2000 ppm. For context, ethanol has been assigned a 1000-d SMAC of 1000 ppm (2000 mg · m^{-3}), though the level on ISS is more tightly regulated to avoid impacts to the water recovery system.

However, using data from a 90 d (390 h) study to establish a safety value for 1000 d (24,000 h) is not consistent with best practice, in the absence of supporting data. Thus, the applicable value for the shorter-term nominal SMACs will be divided by 3 to account for deficiencies in the available data. This results in a 1000-d SMAC of 39 ppm (140 mg · m^{-3}).

DISCUSSION

SMACs have been developed and adopted for ethanol.[38] The long-term SMACs were all set at 1000 ppm (1900 mg · m^{-3}) to protect against irritation of the eye and mucous membranes, along with flushing of skin and the possibility of hepatotoxicity. Hydrolysis of the acetate ester by carboxylesterases present in the nasal mucosa are likely responsible for the irritating effects of ethyl acetate at moderate concentrations (i.e., 400 ppm and greater).

One source of uncertainty is the designation of 350 ppm (from subchronic chamber exposures of rats to ethyl acetate) as a NOAEC in setting of SMACs for 30-, 180- and 1000-d durations. The investigator suggested 350 ppm is a LOEC in the context of lesions in olfactory tissue and in the context of body-weight gain and food efficiency in male rats.[13] With regard to the olfactory lesions, the anatomical differences between humans and rats and rats being obligate nose breathers complicate interpretation of the relevance to human health.[10,27] Also, these lesions were minimal at the 350 ppm dose level and limited to 8 of the 20 exposed animals (3 male, 5 female).

The reductions in body weight gain and food efficiency in male rats only were considered as not physiologically significant by EPA, though they were statistically significant.[23] Female

rats did not experience any significant decreases in body weight gain or food efficiency at the 350 ppm dose level, and the investigators note that this dose is a NOEC for female rats.[12]

Given the short half-life of ethyl acetate in vivo and the nature of the adverse health effects observed by the investigators, the application of this study to SMAC development generates SMAC values that are protective of astronaut health during long-term spaceflight.

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Performance Risks During Surface Extravehicular Activity and Potential Mitigation Using Multimodal Displays

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BACKGROUND: Surface extravehicular activity (sEVA) will be a critical component of future human missions to the Moon. sEVA presents novel risks to astronaut crews not associated with microgravity operations due to fundamental differences in task demands, physiology, environment, and operations of working on the lunar surface. Multimodal spacesuit informatics displays have been proposed as a method of mitigating sEVA risk by increasing operator autonomy.

METHODS: A formalized literature review was conducted. In total, 95 journal articles, conference papers, and technical reports were included. Characteristics of U.S. spacesuits were reviewed, ranging from the Apollo A7L to the xEMU Z-2.5. Multimodal display applications were then reviewed and assessed for their potential in aiding sEVA operations.

RESULTS: Through literature review 25 performance impairments were identified. Performance impairments caused by the spacesuit represented the greatest number of sEVA challenges. Multimodal displays were mapped to impairments and approximately 36% of performance impairments could be aided by using display interfaces.

DISCUSSION: Multimodal displays may provide additional benefits for alleviating performance impairments during sEVA. Utility of multimodal displays may be greater in certain performance impairment domains, such as spacesuit-related impairments.

KEYWORDS: Artemis, Moon, bioastronautics, astronaut, human spaceflight, aerospace.

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Extravehicular activity (EVA) comprises work that astronauts complete outside of the spacecraft or habitat.[53] Surface extravehicular activity (sEVA) occurs when an astronaut completes this work on the surface of a planetary body, near-Earth asteroid, or a natural satellite (e.g., Earth's Moon). Compared to EVA performed in microgravity, sEVA presents distinct challenges[33] and has not been performed since the early 1970s during the U.S. Apollo program. Future sEVA concepts of operations (ConOps) call for astronauts to perform approximately three EVA per week,[2,33] totaling approximately 24 EVA hours per person per week. This is a marked increase compared to current missions and will likely necessitate new operational paradigms. Additionally, the Artemis program outlines long-term surface operations as a paramount goal for lunar operations.[82] These may include long-duration lunar stays of up to 2 wk of at least four crew.[29]

NASA's Human Research Roadmap has determined that any lunar visit/habitation or Martian EVA will require risk reduction associated with injury, compromised physical performance, and reduced cognitive performance before the risk disposition is acceptable.[24] Specifically, it states that "there is a possibility that crew injury and compromised physiological and functional performance may occur" due to the "physiological and functional demands of operating in a self-contained EVA […] suit." Multiple risk factors affect this assessment such as spacesuit habitability and design, task demand and training, and physical and cognitive states.[24]

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To reduce the stressors of sEVA, a focus on improving EVA informatics has grown within the human spaceflight community. In particular, multimodal displays (MMD) have been suggested as a method for improving operator safety and efficiency. MMDs are guided by Wickens'[93] multiple resource theory. This theory asserts that different sensory modalities each have their own resource allocation and processing channels in the brain. This can be leveraged to increase information bandwidth by spreading the amount of information being presented over multiple sensory modalities. MMDs use congruent and complementary sensory cues to pool multiple attention resources together. Within an EVA context, MMDs can be leveraged to improve spacesuit demand, offload task demand, and improve cognitive state. They have been shown to improve alert response time,[17,91] detection and localization of points of interest,[46,90] and improve situation awareness (SA).[45]

Previous MMD research has shown inconsistent improvement in task performance. Meta-analyses of MMD have shown that taskload protocols have not been manipulated in a systematic and reliable manner.[34] Cognitive workload (WL) and its interaction effects with MMDs are not confidently understood.[21,34] MMD research in sEVA has been accomplished by the Human Systems Integration division out of NASA Ames Research Center,[17,46,91] as well as joint investigations between academic institutions and NASA Johnson Space Center.[45] Previous research from these groups has focused on specific applications for sEVA such as navigation or procedure display. It may be possible, though, to use MMDs to mitigate additional sEVA risk due to their broad applicability. To identify whether this the case, a wholistic evaluation of MMDs and their efficacy in alleviating sEVA performance impairments is needed. This research addresses this gap by conducting a literature review on sEVA performance risks and then identifying the degree to which MMDs may mitigate the described performance impairments.

METHODS

A formalized literature review on extravehicular activity was conducted. References were identified by ScienceDirect and NASA Technical Report Server searches covering 1970 to September 2021 using the terms "EVA", "spacesuit", "Apollo", "Performance", "Lunar", and "Martian." In total, 104 journal articles, conference papers, and technical reports were reviewed. Of these, 95 are included in this review article after accounting for duplicated information between journal/conference publications and relevance to topic. Only U.S. spacesuits were reviewed, ranging from the Apollo A7L to the xEMU Z-2.5. From the literature review, impairments to performance were identified and developed into four thematic categories: spacesuit, physiology, environment, and operations. Multimodal display capabilities, previously identified through military, air traffic control, and automobile applications, were then cross-referenced to performance impairments identified.

RESULTS

Performance Impairments

From the literature review, four primary performance impairment categories were identified: spacesuit, physiology, environment, and operations. There were 25 performance impairments identified and listed in **Table I**. The categories used mirror NASA's EVA Risk Diagram,[24] though we have chosen to separate operations into operations and environment because this analysis focuses solely on sEVA, whereas the Risk Diagram encompasses all types of EVA. It should be noted that identified performance impairments may have multiple causal mechanisms; however, in this research we have chosen to categorize performance impairments by their primary impairment category. An expanded discussion of these impairments is described in the following sections.

The first category is spacesuit-induced performance impairments, wherein the physical limitations created by hardware or software impact performance. Spacesuit-induced performance impairments include limited field of view/regard,[31,60,74] helmet fogging/scratching,[9,77,89] ambient noise level,[8,16] sound reflection,[8,16] loss of fine-motor tactility,[19,27,86] reduced applied strength,[65,75,77] hand fatigue,[73,77,85] shifted center of mass,[6,73,74] and limited upper body[5,75] and lower body mobility.[7,12,59]

The second category is physiology-induced performance impairments, wherein physiological adaptations to space impact human operator performance or increased risk of injury.

Table I. Summary of All Performance Impairments Identified from the Literature.

PERFORMANCE IMPAIRMENT	CASUAL MECHANISM	MMD APPLICATION
Limited Field of View	Spacesuit	X
Loss of Fine Motor Tactility	Spacesuit	X
Limited Mobility	Spacesuit	
Hand Fatigue	Spacesuit	
Reduced Applied Strength	Spacesuit	
Helmet Fogging/Scratching	Spacesuit	
Shifted Center of Mass	Spacesuit	
Ambient Noise Level	Spacesuit	
Sound Reflection	Spacesuit	
Altered Proprioception	Physiology	X
Musculoskeletal Deconditioning	Physiology	
Vestibular Deconditioning	Physiology	
Acute Injury	Physiology	
Long Term Injury	Physiology	
Uneven/Hazardous Terrain	Environment	X
Altered Depth Perception	Environment	
Dust	Environment	
Radiation	Environment	
Altered Visibility Conditions	Environment	
Temperature Variation	Environment	
Limited Communications	Operations	X
Limited or Outdated Procedures	Operations	X
Missed Cautions, Warnings, Alarms	Operations	X
Limited Navigation Information	Operations	X
Limited Bandwidth	Operations	

Performance impairments are categorized by EVA causal mechanisms. Potential multimodal display applications and uses for each performance impairment and their causal mechanisms are denoted with the letter 'X'.

Physiology-induced performance impairments include vestibular deconditioning,[25,26,43] musculoskeletal deconditioning,[78,80] altered proprioception,[60] and acute and long-term injury.[12,77,78]

Environment-induced performance impairments are the third category, wherein the specific characteristics of a lunar, Martian, or near-Earth asteroid (NEA) environment impact performance.

Environment induced performance impairments include lack of atmosphere attenuation,[67,73,87] altered visibility conditions,[67] dust,[10,73,89] temperature changes,[67] hazardous terrain,[67,87] and radiation exposure.[76,87] Finally, operations-induced performance impairments include any changes from current microgravity EVA operations protocols which may negatively impact performance, productivity, or safety. Operational induced performance impairments include limited communications,[3,14,51] limited bandwidth,[3,14,51] limited navigational resources,[14,77] limited or outdated procedures,[28] and missed notifications or alarms.[28]

Each of these performance impairments (spacesuit-induced, physiology-induced, environment-induced, operations-induced) is discussed in detail in the following subsections.

Spacesuit-Induced

Astronaut visual perception impairments are considered the highest risk factor[77,87] due to the astronaut's heavy reliance on visual processing. Pressurized spacesuit testing suggests a decrease in field of view (FOV) from unsuited baseline by approximately 30% in horizontal FOV and 21% in vertical FOV.[5,58,60] In current and historical spacesuit helmet designs, FOV restrictions are unevenly distributed across the inferior and superior directions. A significant reduction in inferior direction was shown while the superior direction remained largely unaffected,[58] which future suit designers should take into account when integrating visual features such as heads-up displays or the Displays and Control Unit (DCU).

Further, lack of helmet neck bearings in current and historical extravehicular mobility unit (EMU) designs eliminate any field of regard (FOR) increases for visual perception. Helmet fogging and scratching[9,77,89] also degrade visual signal integrity and require further risk mitigation for future EVA.

The auditory environment is another consideration for performance decrement. Spacesuit-internal hardware generates and reflects noise while environmental noise is not present due to the lack of planetary atmosphere. Nominal internal background noise in Mark III suit testing averaged around 70dB(A).[16] Noise sources can be attributed to portable life support systems (PLSS) fans and pumps, sound reflection via helmet shape, and bearing or mechanical noise due to spacesuit movement.[8,16] During suited walk-back testing in the Mark III, air circulation within the suit resulted in a distinct "swooshing" sound reported by subjects.[16] Spacesuit internal noise reflection studied by Allen[8] and Begault and Hieronymus[16] found a medium to high level of ambient internal background noise in the spacesuit. With the xEMU incorporating an integrated communication system (ICS), ambient noise levels have the potential to interfere with communication intelligibility. Driving requirements for the xEMU's ICS specify a 90% English intelligibility, with early standalone tests suggesting these requirements have been met.[42] At this time, a complete hardware-in-the-loop test has not been conducted in flight-like environments,[42] but initial results are promising.

Tactile perception impairments are another concern. While EVA glove performance has been heavily studied (see Scheuring et al.[77] for a detailed review paper), only two papers were identified[19,86] that specifically included tactility metrics such as two-point discrimination testing, discussed below. Thompson et al.[86] evaluated a series of bumps resembling screw heads using a 4.3 psid pressurized phase VI glove. On average, a 748% increase in force was required to discern the same bump when participants (4 women, 4 men) donned an unpressurized glove relative to a barehanded baseline. A 1015% increase in force was required when wearing a pressurized glove. It is unclear how many participants correctly identified whether a bump was present. Bishu et al.[19] found gender and the level of pressure to be significant factors impacting performance during two-point discrimination testing and mean time for nut assembly and knot tying tasks.

Gas-pressurized spacesuits require the operator to dedicate some portion of their strength into physically flexing the spacesuit. On average, a 15–20% decrease in overall strength was found during pressurized suited testing,[36,65,75] though one study reported up to 90% decreases in grip strength.[13]

Existing NASA human-system integration requirements take a more conservative approach of up to 50% strength decrease during EVA.[28] During pressurized suited trials, maximum voluntary muscle contractility for a 1-s grip hold decreased by nearly 50% after 20–30 repetitions, though rest time between trials was not strictly controlled for.[13] Improper suit fit may cause joint and limb misalignment between the operator and the spacesuit, increasing relative torque forces required to flex the suit.

Additionally, nearly all pressurized suit studies do not account for any musculoskeletal deconditioning during transit or during extended periods of stay in the lunar or Martian environment. A study of 37 International Space Station (ISS) crewmembers who averaged 163 d (±38 d) in microgravity showed that even with an advanced resistive exercise device (aRED), isokinetic strength decreased by an average of 12% across knee and ankle flexion/extension.[36] Stamina and fatigue will become increasingly important during planetary habitation due to an increased frequency of EVA. Fatigue during Apollo has been documented through a series of interviews. Multiple astronauts identified hand fatigue as the primary limiting factor during their EVA.[27,73,85] Suited mobility and work envelope (WE) are largely dictated by suit bearing design and suit fit.

As such, measuring mobility or WE are restricted to specific spacesuit models or even test subjects, making generalized mobility or WE models difficult.[49] Recent advancements in spacesuit modeling have helped to bridge this gap,[30] but literature is still sparse. Alternative measurements for suited mobility based on metabolic costs are being investigated by NASA.[59]

Spacesuit bearing and programming can lead to altered movements and response execution strategies. The hip brief assembly from the Mark III, which will be featured in the xEMU lower torso assembly, has been studied extensively.[7,30,70] There are limitations associated with the Mark III hip brief assembly, primarily attributed to the three separate, single degree-of-freedom bearing design. The human hip joint is separated into three separate bearings in the hip brief assembly, leading to misalignment of joint hinges between the spacesuit and the human body. This results in changes to static and gait parameters, dynamic base parameters, and decreased bent torso stability.[6,30] Poor suit fit can also affect mobility and work envelope, but also contribute to injury, with hand and shoulder injuries occurring most often.[78] Suited injuries have been largely documented in the past,[12,77,78] though specific causal mechanisms are still being investigated.[11] Finally, it should be noted that increased mobility may not be beneficial to all tasks. In microgravity EVA simulations, stiffness of the lower torso assembly allowed astronauts to create more leverage when interacting with the articulating portable foot restraint.[7]

Shifted center of mass from the extravehicular mobility unit and portable life support system introduces risks which may become exaggerated during sEVA. Interviews with Apollo astronauts suggest that although the PLSS created a tendency to tip backward, most astronauts did not have serious problems maintaining balance.[73] However, when attempting to stand up after falling down, the risk of losing one's balance may become more exaggerated.[74] The effects of shifted center of mass in partial gravity environments were not easily assessed through literature. This issue can be studied in a variety of analog settings but remains difficult due to the imperfect nature of these representative environments.

Operational testing in NASA's Active Response Gravity Offload System (ARGOS) have focused on achieving a realistic center of gravity but is not a perfect analog for hypogravity due to harness contact points.[18] Parabolic flights are suitable analogs for hypogravity effects, but can only be achieved for a short duration. Underwater environments such as the Neutral Buoyancy Lab and NASA's Extreme Environment Mission Operations (NEEMO) can be used to study shifted center of mass, but water drag inhibits natural mobility and is prone to similar contact point issues as ARGOS.[18] Ultimately, the tradeoff between PLSS mass and mobility will need to be studied in greater detail.[6]

Physiology-Induced

Atrophy of bones and muscles is the primary risk concern in this category. Risk assessment of bone fracture[66] and compromised physiological performance[24] are currently under investigation by NASA. Bone atrophy in space is not heterogeneously distributed across the body.[52,88,92] Weight-bearing areas such as the hip have seen losses up to 1.7% per month while upper extremities such as the humerus may even gain a small percentage of bone density.[56,69] Muscle atrophy in space follow similar trends to bone atrophy. However, confounds such as diet, exercise level, and stress are difficult to rigorously control for, and may affect the amount of muscular atrophy observed.[20] On average, muscle volume losses in space are greater than what is expected from relevant bed rest studies.[20,55] Antigravity muscles, those involved in posture, such as the quadriceps, hamstrings, and soleus, experience the greatest amount of muscle volume loss in the high teens during long-duration spaceflight.[54] Lower extremity bone and muscle atrophy becomes increasingly important when considering sEVA wherein locomotion is essential to mission operations. Historical EVA data suggest musculoskeletal injuries occur at a rate of 0.26 per EVA.[78] Musculoskeletal deconditioning may also contribute to acute and long-term injury. However, due to multiple contributors to bone and muscle strength, the full impact of spaceflight on the musculoskeletal injury is unknown.[66] Suited fatigue is investigated through a mix of interview reports and strength/stamina studies.[13,27,77] Functional suited tests have been performed,[68] although to the authors' knowledge a functional suited test after being preemptively fatigued has not been performed.

This is an area of ongoing work at NASA. Similarly, the effects of musculoskeletal and vestibular deconditioning and spacesuit strength on functional performance is an ongoing area of interest. To study this effect, a suited functional test could be completed immediately following a bedrest study, though it should be noted that a bedrest study cannot replicate actual unloading of the vestibular system due to the presence of gravity on Earth.[48] Replicating the musculoskeletal loading from hypogravity is also a challenge to performing this kind of evaluation. Further, it is likely that different kinds of spacesuit injuries will occur during planetary ambulation than those accrued in microgravity EVA. Acute and long- term injury have been well documented,[12,77,78] but the causal mechanisms behind some injury hotspots are still unknown. Given the uncertainty around future suit injury paradigms, projecting the overall impact of the effects injury may have on overall mission success will be a challenge. More work is required to categorize the types of injury which can occur during sEVA and their impact on mission goals.

Vestibular perception is important, particularly on early EVA, where decrements are largely attributed to reduced gravity levels. Reduced gravity environments such as the Moon or Mars will introduce a neurovestibular adaptation which may take days or weeks to fully acclimate. Until complete sensorimotor adaption, these environments will induce a number of vestibular perception illusions such as underestimation of roll tilt.[25,26,43] This vestibular perception impairment is most likely to affect manual entry/descent/landing operations or emergency crew egress upon landing. Long-term vestibular adaptation in hypogravity will likely not be an issue for long-duration missions. Altered proprioception due to hypogravity, spacesuit volume, and spacesuit fit may also introduce challenges in future sEVA. Training reports from the Neutral Buoyancy Lab show that trainees often unknowingly bump into the ISS mockup due to lack of awareness because of the PLSS volume or helmet bubble.[60] This challenge may resolve itself after training, but the combined effects of hypogravity, spacesuit volume,

and fit may only be resolved upon arrival to the EVA location due to our inability to fully replicate these effects.

Environment-Induced

Terrain hazards are the primary risk concern in this category. Dust may cause additional hardware-related performance impairments, such as extravehicular visor assemblies not being able to properly retract.[89] Lunar dust kicked up during navigation or routine operations may result in visual gray out[10] or important hardware being covered,[73] as was evident when an Apollo astronaut tore a cable loose from the Lander after accidentally walking over it. Lack of atmosphere attenuation further compounds issues with lunar surface composition, increasing errors in distance estimation and landmark recognition.[67,73,87] Uneven terrain and slopes upward of 30% during sEVA will increase physical WL.[68] Sloped traversal under suited partial gravity loads has limited data,[24] likely due to the high operational cost in order to test. Sloped terrain between 10–30% grade were shown to have a significant impact on metabolic load when ambulating in a spacesuit.[68] Analog environments may be sufficient in assessing the risk associated with this performance impairment, and is an area of ongoing work at NASA.

Planetary extravehicular crew will have to navigate and interact with their surroundings without environmental audio cues to help them maintain SA. External sound cues and effects, such as the Doppler effect, will be entirely nonexistent on the Moon. While sound propagation is present on Mars, any external sound perception will likely be unintelligible to extravehicular crew.[71]

Radiation exposure on planetary surfaces receive some protection when compared to interplanetary flight; however, the risk of high dose-rate exposure is still very high. Low radiation doses may be mitigated by the spacesuit material lay-up, but high-energy radiation is still a concern.[76]

Operations-Induced

Future exploration missions will need a new paradigm for EVA autonomy and self-reliance. Two drivers, one-way light time (OWLT) and limited data bandwidth, have spurred many space-analog missions to study the impact of these restrictions. Although Earth-Lunar OWLT is nearly nonexistent, proposed lunar ConOps have suggested the use of periodic communication models due to extremely high WLs on ground science support teams associated with constant communication models.[94] Further, a Mars-based communication protocol on the Moon allows lunar EVA to act as a proving ground for Martian EVA. OWLT between Earth and Mars ranges from 3–22 min depending on orbit alignment.[63] Two intravehicular crewmembers are likely required under these new conditions, with one focused on timeline operations and the other on science operations.[3,62] Visual-based communication was found to be favored over audio-based communication during the Biologic Analog Science Associated with Lava Tubes (BASALT) research program.[14,51,57] Limited bandwidth of visual imagery has shown mixed results, where one Desert Research and Technology Studies (DRATS) mission resulted in equivalent science data quality between low bandwidth (1.5 mb $\cdot$ s^{-1}, typical bandwidth available through the Deep Space Network) and high bandwidth (6 mb $\cdot$ s^{-1}), though ground science support teams reported higher WL with the low bandwidth condition.[3] Still imagery was found to be more constructive than video feed imagery,[51,57,62] though video feed worked well for SA and still-imagery backup. One study of Mars-based rover operations found little difference in science quality and productivity between a constant communication protocol vs. a 2× daily downlink.[4] However, they note that the twice daily downlink resulted in greater EVA team SA due to greater EVA communication, which occurred less frequently in the constant communication protocol. They attribute this to increased CAPCOM-EV communication during constant communication, which naturally led to less extravehicular team communication.

Many operational challenges associated with the lunar environment are largely based on Apollo interview studies and may represent an incomplete understanding of these performance impairments. These include effects of dust on hardware operation and lack of atmosphere attenuation.[67,87] Lack of atmosphere attenuation was attributed to increased errors in distance estimation and landmark recognition, but interviews from Apollo J-type missions suggest that astronauts may be able to adapt in a few days.[73,87] However, lack of ground-truth data from perceived distances to actual landmark distance decreases the reliability of these findings. These performance impairments may be difficult to study due to scarcity of representative materials (e.g., simulated regolith) on Earth.

DISCUSSION

From the identified performance impairments, the literature on MMDs was reviewed to identify those associated with sEVA that could be at least partially alleviated by MMDs. Of the 25 impairments, 9 were identified, including 2 spacesuit impairments, 1 physiological impairment, 2 environmental impairments, and 4 operationally related impairments. They are identified in Table I. Broadly, it was found that MMD can be leveraged to mitigate impairments through two means: increased safety and greater work efficiency.

Increased levels of SA have been shown to correlate with increased safety.[83] Limited FOV, uneven terrain, altered depth perception, limited navigation information, loss of tactility, vestibular deconditioning, and missed notifications can negatively impact operator SA during sEVA. Several techniques have been suggested as countermeasures for low SA, including SA camera displays,[1,23,45] audio support systems,[32,34,91] and tactile systems.[37,40] SA cameras and visual displays may be easy to implement, but research in this area often assumes a separate support team who analyze the incoming visual information.[32] This makes these types of technologies less promising for real-time SA when considering data bandwidth and one-way light time communication constrictions during Martian EVA (and to a lesser extent, lunar EVA). These types of systems may increase the overall team SA, but more research is required to investigate

the impact on operator SA. Audio-based support systems have been used in a variety of navigation tasks.[35,44,81,84] The primary challenge with navigational aid systems is that they are heavily reliant on GPS, which currently does not exist for lunar operations. In the future, an audio SA support system may be well suited for increasing safety during sEVA if position localization becomes available. Tactile SA systems have been demonstrated in microgravity and shown to improve orientation SA in a weightless, shirt-sleeve environment.[39] Integration with the spacesuit poses challenges given the pure oxygen environment, limited volume to place hardware, and suit-induced tactile impairment against which this information would be overlaid. Ultimately, more research is needed to determine the cost-benefit of a tactile SA system for spacesuit environments. Vestibular stimulation through galvanic vestibular stimulation (GVS) has been studied in translation studies[41] and can be used to improve roll/tilt estimation.[50,95] In theory, GVS has some potential to counteract vestibular readjustment upon landing on a planetary surface but has not been demonstrated in research settings.

MMDs can also improve work efficiency, reducing the total risk exposure in this dangerous environment. Limited communication and outdated or limited procedure information can negatively impact work efficiency during sEVA. Communication between EVA and intravehicular activity (IVA)/ground support (GS) is limited due to data bandwidth and one-way light time constrictions. Reliance on traditional real-time audio communication systems may not be sufficient under these conditions. The primary technology for offloading these performance impairments has been through the visual modality. Providing a text-based messaging system has been shown as a useful method for goal-setting during analog planetary EVA.[32] Additionally, image-based messaging was shown to improve team SA under these contexts. Detailed or "enhanced" procedure information has been investigated by several universities through NASA's university-level challenge (Spacesuit User Interface Technologies for Students).[61,64,72] Subjective feedback from NASA engineers and astronauts through this challenge suggest that incorporating enhanced procedures is useful for EVA.

Importantly, MMDs leverage parallel sensory channel throughput when providing information to the user. However, under highly stressful situations, single channel sensory overload is more likely to happen.[79] Thus, although a multimodal display may be providing more information, the user may not receive the benefits of this increased bandwidth.[22] More research needs to be done in this field specifically as it pertains to space operations. Air traffic control can likely be used as a starting foundation for this research since both exhibit similar operational traits (e.g., high stress, high workload). Literature from air traffic control and multimodal displays suggests that increasing the amount of sensory channels correlates to increased operator SA.[15,38,47]

This research was confined to papers identified through the standardized search approach that was broadly available. Since a great deal of effort may have been performed internally at NASA or related commercial companies, it is possible that these results do not sufficiently capture internal work.

This research identified 25 performance impairments through literature review, divided into four categories of spacesuit, physiology, environment, and operational challenges. Performance impairments caused by the spacesuit represented the largest number of sEVA impairments. Of the 25 identified sEVA performance impairments, 9 were identified as able to be mitigated with MMDs. MMDs can offset multiple types of performance impairment causal mechanisms, but must be done in a manner that does not overly burden the operator's ability to process information. MMDs may serve as a viable candidate for mitigating risk associated with sEVA, but additional research into their ultimate integration for suited operations is needed.

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Measuring Arterial Oxygen Saturation Using Wearable Devices Under Varying Conditions

Eleanor L. Hearn; Jack Byford; Christopher Wolfe; Cheryl Agyei; Peter D. Hodkinson; Ross D. Pollock; Thomas G. Smith

INTRODUCTION: Recently developed wearable monitoring devices can provide arterial oxygen saturation (S_pO_2) measurements, offering potential for use in aerospace operations. Pilots and passengers are already using these technologies, but their performance has not yet been established under conditions experienced in the flight environment such as environmental hypoxia and concurrent body motion.

METHODS: An initial evaluation was conducted in 10 healthy subjects who were studied in a normobaric chamber during normoxia and at a simulated altitude of 15,000 ft (4572 m; 11.8% oxygen). S_pO_2 was measured simultaneously using a standard pulse oximeter and four wearable devices: Apple Watch Series 6; Garmin Fēnix 6 watch; Cosinuss° Two in-ear sensor; and Oxitone 1000M wrist-worn pulse oximeter. Measurements were made while stationary at rest, during very slight body motion (induced by very low intensity cycling at 30 W on an ergometer), and during moderate body motion (induced by moderate intensity cycling at 150 W).

RESULTS: Missed readings, defined as failure to record an S_pO_2 value within 1 min, occurred commonly with all wearables. Even with only very slight body motion, most devices missed most readings (range of 12–82% missed readings) and the rate was higher with greater body motion (range 18–92%). One device tended to under-report S_pO_2, while the other devices tended to over-report S_pO_2. Performance decreased across the devices when oxygenation was reduced.

DISCUSSION: In this preliminary evaluation, the wearable devices studied did not perform to the same standard as a traditional pulse oximeter. These limitations may restrict their utility in flight and require further investigation.

KEYWORDS: pulse oximeter, pilot, hypoxemia, altitude, aviation, spaceflight.

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With a global market size of approximately $40 billion in 2020, wearable technology is a growing industry with a broad impact that is likely to include the aerospace sector.[4] Wearable physiological monitoring devices, or 'wearables', are portable technologies intended to track physiological data such as calories burned, step count, heart rate, and, more recently, arterial oxygen saturation (S_pO_2). Owing to the accessibility and convenience of wearable technology, these devices have the potential to transform remote monitoring in patients at risk of hypoxemia, such as those with chronic obstructive pulmonary disease or COVID-19, and are marketed to consumers as a means of promoting health and well-being.

Aircrew are routinely exposed to mild-moderate hypoxia and, anecdotally, the use of wearables by pilots across general, commercial, and military operations is increasing. Wearable measurements of in-flight S_pO_2 are similarly appealing in other groups such as passengers, aeromedical patients, and skydivers.[1] The ability to detect worsening hypoxemia during flight is highly desirable as it is dangerous and can develop for many reasons, such as reduced cabin pressure, unpressurized flight at high altitudes, pre-existing or acute illness, physical exertion (e.g., helicopter rear crew), high G acceleration, and failure of oxygen delivery and life-support systems. In recent years this

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has been particularly topical in the setting of military fast-jet operations due to the possible contribution of hypoxia to unexplained physiological events. However, it is important to establish the performance of new technologies prior to safety-critical use. With regards to isolated S_pO_2 monitoring during flight, additional care is required as interpretation can be challenging or misleading even for accurate measurements; for example, in the presence of hyperventilation.[2]

While the accuracy of heart rate data from wearables has been well-reported, the ability to measure S_pO_2 is a newer feature and has not been comprehensively investigated.[8] Standard pulse oximeters used in medical practice utilize transmissive photoplethysmography (PPG), in which a light source and photodetector are located on opposite sides of a vascular bed (such as a finger or ear lobe) and the intensity of transmitted light of certain wavelengths is measured. The reliability of this technique is well established, but such devices tend to be somewhat obtrusive when used while performing other activities. In contrast, wearables are by their nature less obtrusive, but typically use the less established technique of reflective PPG, in which the light source and photodetector are positioned on the same side of a vascular bed and the intensity of reflected light is measured.[12] Wearables are also designed for S_pO_2 measurements to be made while completely stationary.

Recently developed wearables that can measure S_pO_2 include consumer-grade products such as the Apple Watch 6 (Apple Inc., Cupertino, CA, USA) and Garmin Fēnix 6 watch (Garmin Ltd, Olathe, KS, USA), which are marketed for 'general fitness and wellness purposes' rather than for medical use. In contrast, the commercially available in-ear ('hearable') Cosinuss° Two (Cosinuss GmbH, Munich, Germany) has undergone testing in clinical settings, although comparative data has not been published and it is not currently classified as a medical device, while the wrist-worn Oxitone 1000M (Oxitone Medical, Kfar Saba, Israel) is an FDA-cleared medical monitor intended for clinical use. The Garmin and Apple watches and Cosinuss° Two use reflective PPG, while the Oxitone 1000M uses transmissive PPG. There is little published research reporting S_pO_2 data from these devices. The Oxitone 1000M has been reported to provide accurate and precise S_pO_2 values when measured in a stationary state,[5] while a recent study conducted in a respiratory outpatient clinic reported the Apple Watch 6 appeared to be a reliable means of measuring S_pO_2 in this controlled setting, although there were occasional outlying values.[10] An earlier Garmin watch model (the Fēnix 5× Plus) was found to over-estimate S_pO_2 in volunteers studied in a normobaric chamber, especially at higher simulated altitudes, and it was noted that achieving a single measurement could take up to 3 min.[6] This highlights the potential for measurement failure to impact on performance—irrespective of its other qualities, a device that is unable to reliably achieve a timely reading is unlikely to be useful in the flight environment.

Although there is limited data and satisfactory performance cannot be assumed across the various technologies, these initial studies are generally encouraging with regards to use while stationary and under normoxic conditions. However, in-flight use does not necessarily allow such optimal conditions; achieving an absolutely motionless state can be challenging or impossible, and a lower range of S_pO_2 may well be encountered. To our knowledge, no previous studies have investigated the potential combined effects of hypoxia and concurrent body motion of any degree. This initial study aimed to undertake a preliminary evaluation of four leading wearable devices in measuring S_pO_2 under normoxic and hypoxic conditions while at rest and during relevant levels of body motion, including very minimal movement only marginally beyond a stationary state. The hypothesis was that their performance in measuring S_pO_2 would be the same as that of a standard pulse oximeter. Our aim was to generate preliminary results and provide a basis for the definitive studies that are ultimately required.

METHODS

Subjects

This study was conducted in healthy volunteers and was approved by the King's College London Research Ethics Committee. It was conducted in accordance with the Declaration of Helsinki. All subjects provided written informed consent.

Equipment

The study was undertaken in a normobaric altitude chamber (Sporting Edge, Basingstoke, UK) containing a cycle ergometer (Monark 818E, Monark Exercise, Vansbro, Sweden). Reference S_pO_2 was measured continuously at the left index finger using a standard pulse oximeter (Pulse Oximeter 7840, Kontron Instruments Ltd, West Sussex, UK) recorded via PowerLab 8/35 and LabChart 8.0 (AD Instruments, Oxford, UK) and was compared with data from an Apple Watch 6 (at the left wrist), Garmin Fēnix 6 watch, and Oxitone 1000M (at the right wrist) and a Cosinuss° Two (in the right ear). All wearables were attached and operated according to the manufacturer's instructions, and the Cosinuss° Two was fitted for size (small, medium, or large). Simultaneous heart rate measurements were recorded from all monitors in parallel with S_pO_2.

Procedure

Subjects attended the laboratory on 2 experimental days separated by a minimum of 24 h. The protocol was identical on each occasion except one day was conducted under normoxic conditions in room air (20.9% oxygen) and the other was conducted in hypoxic conditions at a simulated altitude of 15,000 ft (4572 m; 11.8% oxygen). This altitude was intended to extend nadir S_pO_2 values into the 70–80% range. The order of normoxia and hypoxia was counterbalanced and subjects were blinded to each condition. Following instrumentation, subjects entered the hypoxia chamber and completed 10 min of seated rest. They then cycled on the ergometer for 5-min periods at very low intensity (30 W) and at moderate intensity (150 W) separated by 5 min of seated rest. These periods of cycling were intended as a reproducible means of inducing very slight body motion (30 W) and moderate body motion (150 W), with the added

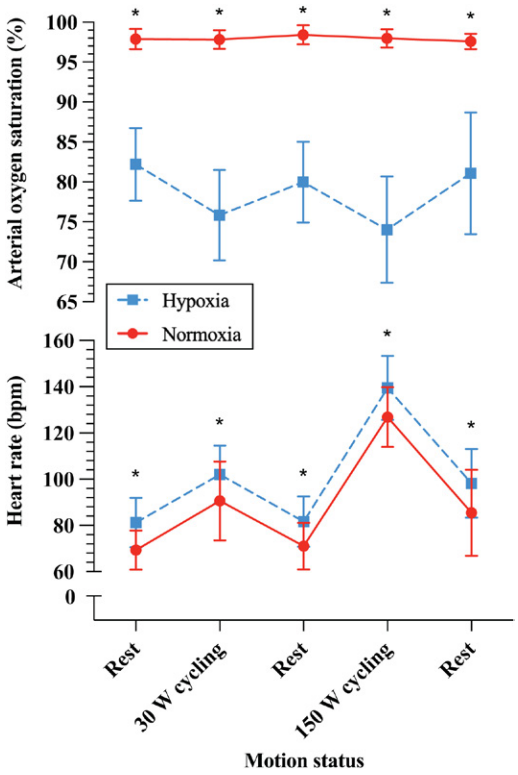

Fig. 1. Mean arterial oxygen saturation and heart rate at rest and cycling at 30 W and 150 W under normoxic (20.9% oxygen) and hypoxic (11.8% oxygen) conditions. Solid red lines and circles denote normoxia. Dashed blue lines and squares denote hypoxia. Asterisks denote a statistically significant effect of hypoxia ($P < 0.05$). Data are mean ± SD.

potential for exaggerating any hypoxemia.[13] Participants were instructed to remain otherwise still while cycling and there was minimal associated motion of the arms and head, especially at 30 W, which requires only very gentle pedaling. A further 5 min of seated rest concluded testing. For each period of rest and cycling, measurements of S_pO_2 and heart rate were recorded at three evenly spaced time points. A maximum of 1 min was allowed to obtain a reading from each device, after which a failed or 'missed' measurement was recorded.

Statistical Analysis

Data were normally distributed (Shapiro-Wilk test). The effect of hypoxia on S_pO_2 and heart rate was analyzed with paired *t*-tests (SPSS Statistics v.26, IBM, Armonk, NY, USA) using mean data for each period of rest or cycling (using S_pO_2 and heart rate data obtained from the reference pulse oximeter). The accuracy and bias of measurements from the wearable devices were tested against the reference pulse oximeter using paired *t*-tests, Bland Altman analyses (GraphPad Prism, v.26, San Diego, CA, USA), and mean absolute percentage error (MAPE) score. MAPE was calculated using the following equation: ((actual value – forecast value)/actual value)*100. Statistical significance was assumed at $P < 0.05$ and data are presented as mean ± SD.

RESULTS

There were 10 subjects (6 men and 4 women) with a mean age of 27 ± 6 yr, weight 75 ± 15 kg, height 1.74 ± 0.11 m, and body mass index 24 ± 3 kg · m^{-2}. **Fig. 1** shows the effects of hypoxia and periods of cycling on the reference physiological data obtained using the standard pulse oximeter. S_pO_2 was significantly lower during hypoxia at rest [82 ± 3% vs. 98 ± 1%; $t(29) = 15.9$, $P < 0.001$], 30-W cycling [76 ± 6% vs. 98 ± 1%; $t(9) = 11.8$, $P < 0.001$], and 150-W cycling [74 ± 7% vs. 98 ± 1%; $t(9) = 12.2$, $P < 0.001$]. There was a small increase in heart rate during hypoxia compared with normoxia at rest [87 ± 14 bpm vs. 75 ± 15 bpm; $t(29) = 6.4$, $P < 0.001$] and similarly during 30-W cycling [102 ± 13 bpm vs. 91 ± 17 bpm; $t(9) = 3.4$, $P = 0.008$] and 150-W cycling [139 ± 14 bpm vs. 127 ± 13 bpm; $t(9) = 2.7$, $P = 0.026$].

Missed S_pO_2 readings were common for all devices, with a progressive increase in the percentage of missed readings with increasing cycling intensity (**Table I**). At rest, the percentage of

Table I. S_pO_2 Measurements: Number of Data Points, Percentage of Missed Readings, Mean Absolute Percentage Error and Percentage Accuracy for Each Device Measuring S_pO_2 at Rest and During Cycling at 30 W and 150 W.

	APPLE WATCH 6	GARMIN FĒNIX 6	COSINUSS^O TWO	OXITONE 1000M
Number of data points				
Rest	160	160	160	160
30-W cycling	60	60	60	60
150-W cycling	60	60	60	60
Missed readings (% of total)				
Rest	2.5%	20%	11%	14%
30-W cycling	65%	65%	12%	82%
150-W cycling	95%	83%	18%	92%
Mean absolute percentage error				
Rest	–2.26	–2.19	2.66	–2.39
30-W cycling	–0.80	–3.92	2.06	–3.44
150-W cycling	–4.21	–9.89	3.33	–6.69
Accuracy (%)				
Rest	97.7	97.8	97.3	97.6
30-W cycling	99.2	96.1	97.9	96.6
150-W cycling	95.8	90.1	96.7	93.3

Table II. Heart Rate Measurements: Number of Data Points, Percentage of Missed Readings, Mean Absolute Percentage Error (MAPE) and Percentage Accuracy for Each Device Measuring Heart Rate at Rest and During Cycling at 30 W and 150 W.

	APPLE WATCH 6	GARMIN FĒNIX 6	COSINUSº TWO	OXITONE 1000M
Number of data points				
Rest	160	160	160	160
30-W cycling	60	60	60	60
150-W cycling	60	60	60	60
Missed readings (% of total)				
Rest	0%	2%	7%	5%
30-W cycling	0%	2%	12%	67%
150-W cycling	0%	0%	20%	77%
Mean absolute percentage error				
Rest	1.05	0.8	7.64	2.56
30-W cycling	−7.51	7.91	0.51	9.71
150-W cycling	−2.33	29.41	45.14	33.32
Accuracy (%)				
Rest	98.95	99.2	92.36	97.44
30-W cycling	92.49	92.09	99.49	90.29
150-W cycling	97.67	70.59	54.86	66.68

missed readings ranged between 2.5% and 20%, while during very low intensity cycling at 30 W, when associated body motion was very minimal, most devices missed most readings (range 12–82%). During moderate intensity cycling at 150 W, the percentage of missed readings ranged between 18% and 95%. Overall, the percentage of missed readings was lowest for the Cosinussº Two and highest for the Oxitone 1000M. MAPE and percentage accuracy were calculated and are shown in Table I. With increasing cycling intensity, MAPE increased and percentage accuracy decreased. The Apple Watch 6 displayed the highest percentage accuracy independent of motion status, while the Garmin Fēnix 6 showed the lowest percentage accuracy. Equivalent data for heart rate is shown in **Table II**. Missed heart rate readings were generally less frequent, while overall, from rest to 150-W cycling, MAPE increased and percentage accuracy decreased.

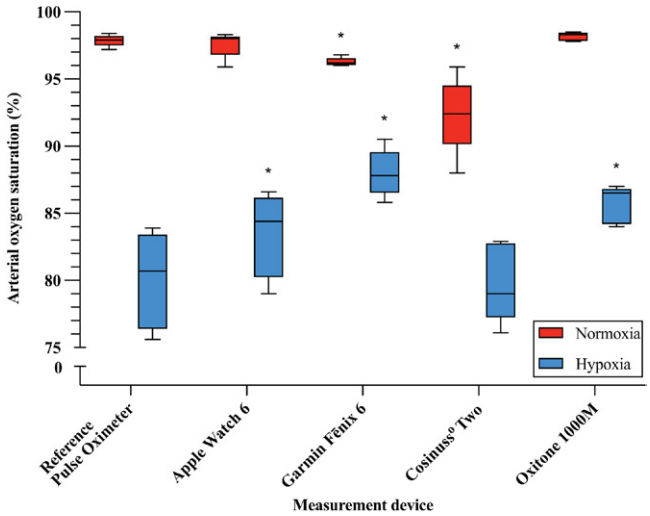

Fig. 2. Arterial oxygen saturation measured by the reference pulse oximeter and wearable devices during normoxia (red boxes) and hypoxia (blue boxes). Data are from all conditions combined (rest and cycling). The mean, interquartile range (boxes) and maximum and minimum values (bars) are shown. Asterisks denote a statistically significant difference ($P < 0.05$) between reference data obtained from the traditional pulse oximeter and data from the respective wearable devices.

Fig. 2 shows all recorded S_pO_2 data (at rest and while cycling) for each of the respective devices during normoxia and hypoxia. Under normoxic conditions, when values were successfully obtained, the S_pO_2 data from the Apple Watch 6 [$t(4) = 0.5898$, $P = 0.6$] and Oxitone 1000M [$t(4) = 1.215$, $P = 0.3$] were not significantly different from reference data obtained from the traditional pulse oximeter. However, S_pO_2 readings from the Garmin Fēnix 6 [$t(4) = 4.867$, $P = 0.008$] and Cosinussº Two [$t(4) = 3.964$, $P = 0.017$] were significantly different from the corresponding reference data. During hypoxia, the Cosinussº Two [$t(4) = 0.3653$, $P = 0.7$] was the only device to provide S_pO_2 measurements that were not significantly different from the reference data; the Apple Watch 6 [$t(4) = 8.025$, $P = 0.001$], Garmin Fēnix 6 [$t(4) = 4.094$, $P = 0.015$], and Oxitone 1000M [$t(4) = 3.812$, $P = 0.019$] data were significantly different from the reference data. Equivalent data for heart rate is shown in the supplementary online appendix (**Fig. A1**, found with the online version of this article or at https://doi.org/10.3357/AMHP.6078sd.2023).

Overall, when normoxic and hypoxic measurements were combined, the Apple Watch 6, Garmin Fēnix 6, and Oxitone 1000M all tended to over-report S_pO_2 both at rest and while cycling, while the Cosinussº Two tended to under-report S_pO_2 (**Fig. A2**, found with the online version of this article or at https://doi.org/10.3357/AMHP.6078sd.2023). Compared with the reference S_pO_2 data, the Apple Watch 6 had the smallest mean bias (rest: 1.7 ± 2.1%; 30-W cycling: 1.2 ± 3.4%; 150-W cycling: 1.9 ± 2.3%), while the Cosinussº Two had the largest mean bias (rest: −2.9 ± 3.0%; 30 W: −1.5 ± 3.7%; 150 W: −6.5 ± 5.2%). The Oxitone 1000M over-reported S_pO_2 with a higher mean bias (rest: 2.0 ± 1.8%; 30 W: 3.4 ± 3.8%; 150 W: 5.3 ± 6.5%) during cycling compared with at rest (Fig. A2). Equivalent data for heart rate is shown in the supplementary online appendix (**Fig. A3**, found with the online version of this article or at https://doi.org/10.3357/AMHP.6078sd.2023).

DISCUSSION

This preliminary study of four wearable devices indicates that, across a range of S_pO_2 values and levels of body motion, the ability of each of the respective devices to measure S_pO_2 diverged substantially from that of a traditional pulse oximeter. A high proportion of readings were recorded as 'missed' when the device failed to provide a measurement within 1 min, which would be considered a potentially critical operational failure in many aviation contexts. Missed measurements were common even at rest for most devices and none were able to reliably provide S_pO_2 measurements during cycling at moderate or even low intensity, when associated movement of the rest of the body was very minimal. The Apple Watch 6 had the highest accuracy with a potentially acceptable bias when S_pO_2 values were achieved, but the device missed the majority of readings in the presence of very slight body motion, and missed nearly all readings when body motion was at a moderate level. These wearable devices are designed for S_pO_2 measurements to be taken in a stationary state, but this is likely to be difficult or impossible to achieve during flight operations. Measurements were frequently missed even when there was only the slightest body motion and it is, therefore, questionable whether these devices would be able to obtain measurements reliably in many real-world settings, including aerospace environments.

The reduction in the performance of wearables in the presence of any movement of the body is attributable to motion artifact. As technology advances and becomes progressively miniaturized, this more readily exposes the PPG signal to noise such as motion artifact and movement of the PPG sensor that alters the direction in which the light signal is emitted. This is particularly pertinent when the motion artifact frequency corresponds with that of the PPG signal (0.5–5.0 Hz). Typically, motion artifact noise relates to a frequency of 0.01–10 Hz, thus regularly overlapping with the PPG band.[7]

A further factor to be considered is the potential for variation in peripheral circulation to affect S_pO_2 measurements. Poor perfusion can cause a decrease in the ratio of arterial to venous blood at the sensor location, reduced venous saturation through a larger oxygen extraction ratio, and lower pulse amplitude. In addition, motion artifact can have a more profound impact when pulse amplitude is suppressed as it exerts a greater influence on the PPG signal.[9] Poor perfusion could conceivably have lowered the S_pO_2 readings of the wrist-worn wearables in this study if a redistribution of blood flow to the exercising muscles in the lower limbs occurred. However, this seems unlikely as any such effect would also have applied to the reference pulse oximeter, and we note that the Cosinuss° Two (situated in the ear) was the only device to consistently under-report S_pO_2.

The performance of wearables in measuring S_pO_2 has only been investigated in a small number of studies in which data was obtained at rest.[5,6,10] A perfectly motionless state provides optimal conditions and may explain the more favorable comparative data obtained with the Apple Watch 6,[10] Oxitone 1000M,[5] and the predecessor Garmin Fēnix 5× Plus watch.[6] The latter study also explored the effect of reducing inspired oxygen concentration and demonstrated a larger bias at a simulated altitude of 12,000 ft (3658 m) compared with lower altitudes.[6] In the current study we observed a decrease in the performance of S_pO_2 measurements under hypoxic conditions compared with during normoxia in all four wearable devices. Pulse oximeter performance is known to be reduced at lower S_pO_2 values[11] and, in this context, the possibility that wearables may be additionally unreliable when oxygenation is lower, such as at altitude, warrants particular caution regarding their use in aerospace operations.

This study had several limitations. The sample size was intended to allow an initial preliminary evaluation of multiple wearables across varying conditions. The results are preliminary in nature and are intended to serve as the basis for more definitive research. Subjects were young and healthy and were primarily from a white ethnic background, precluding any analysis of the effect of skin pigmentation.[3] Cycling does not replicate actual in-flight conditions and was used as a reproducible surrogate for relevant levels of body motion, as this is the aspect of pedaling that has the potential to impair readings from wearable devices. The protocol did not target associated metabolic activity, which is not directly related to the function of wearable monitors. It should be noted hardware and software for these technologies remain under continuing development and improvement. Furthermore, consumer grade products such as the Apple Watch 6 and Garmin Fēnix 6 carry disclaimers that S_pO_2 readings are not intended for medical use and associated product information acknowledges various factors may affect measurements, including a user's individual anatomy, the fit of the device, and ambient light conditions.

Wearable technology is rapidly advancing and, with further development, the ability to measure S_pO_2 unobtrusively offers great potential to be useful in a multitude of settings, including as a means of early detection of hypoxemia in clinical populations. This could encompass ambulatory and outpatient settings as well as ward-based, perioperative, and critical care medicine. Ultimately, wearable-derived S_pO_2 data may likewise offer benefits as in-flight tools, whether for pilots, passengers, aeromedical patients, rear crew, or skydivers. Based on this preliminary study, we suggest further research and development is required before this can be generally recommended. Future investigations may consider ways to minimize movement-associated noise infiltrating reflective PPG signals and should encompass relevant populations and environmental conditions, including actual in-flight measurements.

In summary, while wearable devices offer great promise, in this preliminary study the four wearable devices investigated did not perform to the same standard as a traditional pulse oximeter for S_pO_2 measurements. Limitations associated with varying conditions, including minimal body motion, may well apply in real-world settings, including aviation and spaceflight, and further research into the use of wearables in these domains is required.

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Implantable Collamer Lens Use in a Spaceflight Participant During Short Duration Spaceflight

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BACKGROUND: The purpose of this report is to document the first use of a single piece, posterior chamber phakic implantable collamer lens (ICL) with a central port in the right eye (OD) of a spaceflight participant (SFP) during a 12-d Soyuz mission to the International Space Station (ISS). We also briefly document the stability of a pre-existing pachychoroid pigment epitheliopathy (PPE) in the macula of his left eye (OS) during this mission.

CASE REPORT: Ocular examination, including refraction, slit lamp examination, macular examination by optical coherence tomography (OCT), and tonometry were performed before and after his mission and he was questioned regarding visual changes during each portion of his flight.

DISCUSSION: We documented no change in ICL position during his spaceflight. He reported stable vision during liftoff, entry into microgravity, 12 d on the ISS, descent, and landing. Our results suggest that the modern ICL with a central port is stable, effective, and well tolerated during short duration spaceflight. His PPE also remained stable during this mission as documented by OCT.

KEYWORDS: implantable collamer lens, pachychoroid pigment epitheliopathy, vision, spaceflight.

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During spaceflight the eyes of astronauts are exposed to an extremely unique microgravity environment that may result in a spectrum of ocular anatomic changes including optic disc edema, flattening of the posterior globe, choroidal expansion, shallowing of the anterior chamber (AC) with anterior movement of the iris, and alterations in aqueous flow.[4,5,7] These microgravity-induced changes, as well as increased G forces during takeoff and re-entry, have the potential to impact the position and associated optical stability of an implantable collamer lens (ICL). Also, the expanding choroid during microgravity exposure could potentially exacerbate pre-existing pachychoroid pigment epitheliopathy (PPE). In this report we document the first successful use of an ICL (OD) during 12 d of spaceflight onboard the International Space Station (ISS). We also briefly describe the stability of a mild, pre-existing PPE OS in this same spaceflight participant (SFP) during this mission.

CASE REPORT

The spaceflight participant, a 46-yr-old Japanese man, had a Visian implantable collamer lens with CentraFLOW KS-AquaPORT technology implanted OD on December 18, 2017, in Japan. His preoperative refractive errors were −0.75–1.00 × 085 OD and −1.00–0.50 × 070 OS, correctable to 20/13 OD and 20/10 OS. His postoperative course OD was uneventful with 20/16 uncorrected distance visual acuity, a 1-mo postoperative refraction of plano-0.50 × 075 correctable to 20/10, a central corneal thickness (CCT) of 595 μ, an ICL vault of 0.20 CCT, and a tonometry reading of 16 mmHg. In December 2020, a 3-yr postoperative eye exam documented uncorrected distance visual acuity 20/40 OD and 20/50 OS with refractive errors of −1.00–0.75 × 075 OD and −1.50–1.00 × 075 OS, correctable to 20/10 OD and 20/12 OS, with an ICL vault of 0.16 CCT. He had a history of subfoveal retinal pigment epithelium (RPE) irregularities from mild previous

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central serous chorioretinopathy (CSC) OS with no history of decreased vision or metamorphopsia.

A pre-mission eye examination, performed in Houston, TX, USA, 3 mo prior to his December 2021 flight documented an uncorrected visual acuity of 20/40 OD and 20/100 OS, with manifest refractions of −1.25–0.25 × 075 OD and −1.75–0.75 × 075 OS correcting to 20/20 OU. His Goldmann tonometry readings were 14 mmHg OD and 15 mmHg OS. His corneas and irises were clear OU. A properly positioned ICL with a central hole was present OD. His dilated fundus exam noted lens nuclear sclerosis and cortical changes OD and clear OS. This new onset of nuclear sclerosis since his 2017 ICL insertion was thought to be responsible for his myopic shift and he was prescribed single vision distance glasses for correction. The vitreous and AC were clear OU. His optic discs and retinal vasculature were normal OU. Macular optical coherence tomography (OCT) (Heidelberg Spectralis, Franklin, MA, USA) documented a thickened choroid OU with mild RPE changes OS consistent with PPE with no evidence of subretinal fluid.

His last preflight eye examination was performed in Star City, Russia, 20 d before launch. At this time, his autorefraction (Huvitz Charops MRK-3100P autorefractor keratometer; Huvitz, Gyeonggi-do, Republic of Korea) was −1.00 sph OD, and −1.75 sph OS with each eye correctable to 20/20. His noncontact tonometry (Reichert AT 550) was 14 mmHg OU. He launched on a Soyuz spacecraft from the Baikonur Cosmodrome in Kazakhstan on December 8, 2021, on a 12-d Russian mission to the ISS. During private medical conferences held on Flight Days 2, 3, 7, and 11, he was routinely asked about visual changes. He denied any change in vision or ocular discomfort throughout the mission. Given the largely near vision environment on the ISS, he only used his single vision distance glasses to look out the window from his crew quarters. No in-flight testing was planned or performed.

He also experienced no visual changes during his atmospheric entry in the Soyuz Descent Module that reached a deceleration of more than +4.0 G_x (eyeballs in) or during the parachute-assisted landing in Kazakhstan. Following return to Star City on the same day, a basic eye exam was performed and demonstrated uncorrected visual acuity 20/16 OU at 1 m. One day after return autorefraction was −1.25 sph OD and −1.75 sph OS, correcting to 20/20 in each eye at distance. There was no change in his cornea, iris, or lens from his pre-mission examination and slit lamp examination confirmed no post-flight change in ICL position. His fundus exam was normal OU and there was no change in macular appearance on OCT OU. His noncontact tonometry was 15 mmHg OD and 16 mmHg OS. Optic discs were normal OU with no evidence of edema. A follow-up exam was performed in Japan 18 d after return. On this visit his uncorrected distance visual acuity was 20/30 OD and 20/80 OS with manifest refractions of −0.75–0.50 × 050 20/10 OD and −1.50–1.00 × 060 20/10 OS, an ICL vault of 0.10 CCT and tonometry readings of 16 mmHg OD and 18 mmHg OS. The remainder of his eye exam was unchanged and he had no visual complaints.

DISCUSSION

Intraocular lenses (IOL) can trace their origin to World War II aviation. During the Battle of Britain, in 1940, fragments of Plexiglass from the shattered canopies of British Hurricane and Spitfire aircraft sometimes became lodged within the eyes of pilots. The British ophthalmologist Harold Ridley (later to become Sir Harold Ridley) carefully monitored these plastic intraocular splinters and determined that they produced little or no inflammation.[1] This led to the concept that an intraocular plastic lens of the proper size and power could potentially restore vision following the removal of an opacified natural lens. Ridley became the first to surgically implant an IOL in a human in 1949.[1] This landmark surgical procedure set the stage for the gradual evolution and improvement of IOL design and surgical techniques. The first use of IOLs in terrestrial aviation was reported by the U.S. military in 1987.[6] IOL use was subsequently documented in an astronaut during a 2-wk space shuttle mission in 1999[9] and during a 6-mo ISS mission in 2018.[8] These reports documented stable vision and position of IOLs inserted within the capsular bag following the surgical removal of a cataractous lens by phacoemulsification. It is important to note that IOL capsular bag stability was demonstrated even following the emergency ejection of an aviator from a high-performance U.S. Air Force aircraft.[11] Currently, this type of capsular bag fixated IOL can be approved for use in flight personnel in all four military services and the NASA astronaut corps.

The surgical approach, insertion, and positioning of the ICL contrasts with the standard phacoemulsification/IOL surgery used in the above reports. In the ICL procedure, a 3.0–3.4 mm clear cornea tunnel incision is made at the corneal limbus on the steep meridian using topical or peribulbar anesthesia. The foldable Visian ICL is then injected into the posterior chamber between the iris and crystalline lens with support from the ciliary sulcus. Although this procedure has demonstrated postoperative safety and stability for the correction of myopia in the terrestrial environment,[2,10] this is the first report of ICL use during spaceflight.

The insertion of an ICL in an astronaut raises several potential concerns related to the interaction of the lens implant with the changing anatomy and physiology of the posterior chamber during spaceflight. Within seconds of exposure to microgravity, there is a sudden expansion of the choroid. Several studies have quantified this choroidal expansion using OCT during long-duration spaceflight.[4,5,7] This choroidal expansion may cause an anteriorly directed force on the vitreous, a concomitant anterior movement of the crystalline lens, and some narrowing of the AC. A study by Macias et al.[5] demonstrated peripapillary choroidal expansion during and after 6 mo of spaceflight. Although equipment for AC measurement was not available during spaceflight, AC narrowing was also documented following 6 mo of spaceflight in these normal phakic astronauts.[5] These spaceflight-induced anatomical changes could potentially adversely impact the position of an ICL during spaceflight as well as the status of a preexisting maculopathy.

In phakic terrestrial patients, safety concerns related to ICL vault and positioning include the potential for pupillary block with elevated IOP, corneal endothelial cell loss, iris pigment dispersion, and anterior subcapsular cataract formation.[10] Given the ocular physiological changes that occur during spaceflight, these concerns are magnified in astronauts. In an astronaut with an ICL, even a slight anterior displacement of the crystalline lens during microgravity exposure could set the stage for pupillary block and pathologically elevated IOP. Early ICL versions with no central opening were of particular concern, even in the terrestrial environment, and necessitated the need for prophylactic laser peripheral iridotomy. However, the addition of a 0.36-mm central hole in the Visian ICL allows for free aqueous flow through the ICL and has largely addressed the potential for pupillary block in terrestrial patients.[2,10] This central hole also improves aqueous circulation and decreases the incidence of cataracts with no effect on vision.[2,10] Proper vaulting (central separation between the ICL and the anterior surface of the natural lens) is essential to allow adequate separation between the ICL and the anterior lens capsule to avoid the formation of an anterior subcapsular cataract. The degree of vault is related to the interaction of the ICL with the anatomy and physiology of the posterior chamber.[10] Current vault recommendations based on the nonfenestrated version of the ICL are for 50–100% central corneal thickness or 250 μ to 750 μ with a maximum recommendation of 1000 μ. There are no published changes to the guidelines for the fenestrated ICL. Given this SFP's normal postflight intraocular pressure (IOP), lack of symptoms suggestive of elevated IOPs, clear anterior lens capsule, and stable vision, it appeared that the central hole, ciliary sulcus fixation, and vaulting in his ICL permitted sufficient free flow of aqueous to avoid pupillary block and lens contact during spaceflight.

An increase in episcleral venous pressure also occurs during head-down tilt, parabolic flight, and microgravity exposure and may impact AC aqueous volume. However, since the aqueous outflow is only approximately 3 $\mu L \cdot min^{-1}$, this process would not account for the quick spike in IOP noted in analog and microgravity studies. More likely, as the choroid is drained by the vortex vein system and largely not autoregulated, craniocervical venous congestion may inhibit choroidal drainage and lead to a sudden expansion of relatively stagnant blood in the choroid and a concomitant quick rise in IOP.[7]

Greenwald reported choroidal thickness increased during long-duration spaceflight using a single OCT B scan aligned through the fovea and optic disc.[3] Choroidal expansion during spaceflight is also hypothesized to set the stage for choroidal folding, which is well documented.[7] This SPF's preexisting PPE and macular RPE irregularity could theoretically predispose him to CSC from the anterior force created from increased choroidal expansion during spaceflight. Since CSC is caused by leakage from the choroid through a defect in the RPE,[12] spaceflight-induced choroidal expansion might exacerbate this condition. However, we noted no change in his macular RPE status or evidence of subretinal fluid after 12 d of microgravity exposure.

This report describes the first use of an ICL during spaceflight. Following spaceflight, we documented no change to the iris or lens and no change in ICL position. Stable vision during launch, entry into microgravity, 12 d of spaceflight, re-entry, and parachute-assisted landing in this SFP suggests that the low mass, sulcus fixation, central port, and vaulting of the ICL protected it from displacement. Our report suggests that the ICL with a central port is stable, safe, and effective during short-duration spaceflight. Also, this SFP's preexisting PPE was not exacerbated by choroidal expansion during this short-duration spaceflight.

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JANUARY 1998

Human performance in extended isolation (U. of California San Diego, La Jolla; East Carolina U., Greenville, NC; U. of Connecticut, Storrs, CT; Texas Tech U., Lubbock): "Evidence of a specific pattern of performance decrement in isolated and confined (ICE) environments has not been consistently demonstrated in previous research… Decrements in performance in ICE environments: a) occur in a linear, dose-response manner; b) occur in stages; or c) do not occur at all… There were 83 members of the United States Antarctic Program who spent an austral winter at the Amundsen-Scott South Pole Station (90°S between 1991 and 1994 and completed the Profile of Moods States (POMS) once a month for an 8-mo period from March through October… Over the entire 8-mo period, there was a decline in depression ($p = 0.007$) and vigor ($p < 0.0001$), and an increase in fatigue ($p = 0.059$) and tension-anxiety ($p = 0.075$). Of these four measures, only vigor exhibits a linear pattern. Mean scores for tension-anxiety and fatigue were lower during the first half of the winter than the second half ($p = 0.074$ and 0.077, respectively). In comparisons between each quarter and the remaining three quarters, averaged mean tension-anxiety scores and fatigue scores were lower during the second quarter ($p = 0.009$ and 0.03, respectively), and higher during the fourth quarter ($p = 0.025$ and 0.035, respectively) than during the previous three quarters combined… The duration of optimal performance in isolated and extreme environments and the explanation for changes in performance during long duration assignments in such environments both depend on what behavioral measure is used to assess performance."[4]

JANUARY 1973

Aviation medicine and the aviation industry (Aviation Insurance Agency, Atlanta Airport, Atlanta, GA): "In looking into the future of civil aviation medicine, the present structure of the specialty is reviewed in its relationship to the industry and is related to its function as a minimal monitoring system. The need for standardization and expansion are presented as basic requirements to enable aviation medicine physicians and airline medical departments to increase their productivity in the airline industry.

"As the specialty expands with standardization, various functional goals are suggested to strengthen the inter-relationship with airline management, pilots and airline safety. Examples are given and emphasis is placed regarding: (a) Preventive and educational medicine. (b) Operational aviation safety. (c) Development of the 'crew concept'. (d) Revision of aeromedical standards based on actual job performance related research."[3]

Oculogravic studies (Naval Air Development Center, Warminster, PA): "The Naval Air Development Center's human centrifuge was used to generate acceleration profiles approximating those encountered in aircraft catapult launchings. Twelve subjects attempted to keep a continuously moving target at subjective eye level before, during, and after exposure to the accelerations. Our results showed that subjective eye level was changed by exposure to the accelerations, and that, in some individuals, the change persisted for more than 1 minute after the simulated launch sequence was completed. The results are discussed in terms of the effects of rotated acceleration vectors on human spatial orientation, and the data are related to certain types of aircraft losses that have been reported following catapult launchings at night."[1]

JANUARY 1948

Future of postwar aviation medicine (written by U.S. Army Air Forces as bill was establishing USAF): "We are in the postwar period. We longed for these days when actual combat would no longer direct our decisions, and we could turn to a consideration of our long-range program in aviation medicine. Now we are again under duress. There are several problems that face us in this difficult period of readjustment. The airlines are having a severe financial testing. The aircraft industry has withstood staggering blows and the flow of planes is almost stopped. These are stormy days, but the storm will blow over. Our national security requires the best Air Force in the world. Civil aviation will achieve its proper place as the principal means of transportation, both internationally and within the United States; therefore, it is necessary to define the scope of the medical service needed to support this great enterprise…

"In order to establish in the minds of the medical profession at large the proper position of aviation medicine, it is suggested that this Association form a Board for certification of properly qualified doctors in the specialty of aviation medicine…

"I think the time has come when this Aero Medical Association should adopt standards for certification in aviation medicine and proceed with the formation of a competent board recognized by the American Medical Association and operating conjointly with the American Medical Association…

"Another problem which is not peculiar to the military is that pressing need for research in the human abilities in flight. The Army Air Force carries out an extensive program of aviation medicine research, both in its own laboratories and by contract with universities. The Office of Naval Research and The Bureau of Medicine and Surgery are engaged in a similar program. This research in the human equation in aviation is of paramount importance in the design of future aircraft."[2]

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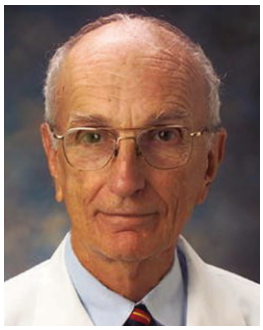
In Memoriam: Frank Pettyjohn

AsMA Headquarters staff were deeply saddened to hear of the death of Dr. Frank Pettyjohn, a Fellow of the Aerospace Medical Association, in early December. A native of Delaware, Dr. Pettyjohn graduated in 1956 from the University of Delaware with a B.S. in Civil Engineering. He subsequently entered the U.S. Army as a 2nd Lieutenant in the Corps of Engineers. Following a tour in Korea, he returned to attend Hahnemann University School of Medicine, Philadelphia, PA, graduating in 1963 with an M.D. degree. After an internship at Madigan Army Medical Center, Fort Lewis, WA, he attended the U.S. Navy School of Aviation Medicine and then the U.S. Army School of Aviation. He received his designation as a Naval Flight Surgeon and an Army Flight Surgeon and served his initial Flight Surgeon tour at Simmons Army Airfield, Fort Bragg, NC.



Dr. Pettyjohn then served in Vietnam as a Flight Surgeon for the 17th Combat Aviation Group in 1966. Upon his return, he entered internal medicine residency training at Madigan Army Medical Center, Fort Lewis, WA. He then began initial residency training in aerospace medicine as a Post Doctoral Fellow in Public Health Preventive Medicine at the University of Washington, Seattle, WA. He returned to Madigan Army Medical Center to complete a Fellowship in Cardiology. He completed his residency in aerospace medicine at Brooks Air Force Base in 1973. During 1973, he served as Cardiologist and Flight Surgeon for Operation Homecoming to return Vietnam POWs to the United States. He joined the U.S. Army Aeromedical Research Laboratory at Fort Rucker, AL, in 1973. During his research there, he joined the International Academy of Aviation and Space Medicine, where he served as Chancellor from 1998-2003, 1st Vice President in 2003-2005, and President in 2005-2007.

In 1977, Dr. Pettyjohn became Deputy Commander/ Chief, Professional Services, at the U.S. Army Aeromedical Center and Lyster Army Community Hospital, Fort Rucker, AL. He also served as the Commander, U.S. Army Aeromedical Activity. In 1980, he moved to the Naval Aerospace Medical Research Laboratory in Pensacola, FL, as Director of the Applied Aeromedical Research Program. In 1982, he became Commanding Officer, U.S. Army Medical Department Activity and Winn Army Community Hospital, Fort Stewart, GA. In 1985, he returned to the Naval Aerospace Medical Institute in Pensacola, FL, as Cardiologist and Army Liaison Officer until 1986, when he joined the University of South Alabama College of Medicine, Mobile, AL, as a Professor. He was Chairman of the Department of Emergency Medicine for the University of South Alabama Medical Center. He also served as a Cardiology Consultant to the Federal Aviation Administration and as the Medical Director of the Emergency Medical Services Department of Education, College of Allied Health and Professions for the University of South Alabama. Additionally, he was the Medical Director for the Gulf Coast Region VI Emergency Medical Services.

Dr. Pettyjohn was recalled to the U.S. Army in 1991 as a Cardiologist and Aviation Medicine Consultant at the U.S. Army Aeromedical Center during Operation Desert Shield/Desert Storm. He was a member of the team that returned the U.S. POWs from Desert Storm to the United States. In December 2008, he again returned to active duty in the U.S. Army as a Flight Surgeon and Cardiologist with the 345th Combat Support Hospital in Tikrit, Iraq. He returned to the University of South Alabama in 2009. He retired as a Professor Emeritus in 2017.

Dr. Pettyjohn's military awards included the Combat Medical Badge, the Legion of Merit, Bronze Star, Meritorious Service Medal, Air Medal with two oak leaf clusters, U.S. Army Commendation Medal, U.S. Navy Commendation Medal, and U.S. Air Force Commendation Metal. He was the first recipient of AsMA's John Ernsting Award for his long career in aerospace medicine in 2010. He was a member of the Civil Aviation Medical Association and the U.S. Navy Aerospace Medicine Residency Advisory Committee. He served on the Executive Council of AsMA from 1979-1982. He was a Fellow of the American College of Cardiology, the American College of Physicians, and the American College of Chest Physicians. He also served as a reviewer for Aviation, Space, and Environmental Medicine (now known as Aerospace Medicine and Human Performance), AsMA's journal.

AsMA Mentioned in News Report

The Aerospace Medicine Association (AsMA) was mentioned in a report on CBS's Nightly News. The story was on an 11-year-old girl who had an allergic reaction during a flight. The airline did not have an EpiPen in their Emergency Medical Kit (EMK), though they did have epinephrine. Fortunately, there was a doctor on the flight who was able to measure out the dose needed and gave it to the girl. AsMA's recommendations that airline EMKs carry additional items such as auto-injectors and pediatric doses of epinephrine is mentioned a few paragraphs down. The story goes on to discuss what each of seven major airlines said about their EMKs. The full article can be found at https://www.cbsnews.com/news/in-flight-emergencies-airlines-medical-kit-requirements/.

Ever Upward

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