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Our Great AsMA Staff—Highlight on the Home Office

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

Our organization is very fortunate to have a wonderful group of professional staff guiding and serving us on a daily basis! While these individuals are often acknowledged and thanked for their AsMA support during the Opening Ceremony of the Annual Scientific Meeting and at the Honor's Night dinner, most members do not know all of them personally. It is my intent to *shine a light* on the Home Office staff so you may appreciate their backgrounds, duties, commitment, and professional pride.

Gisselle Vargas is currently the AsMA Deputy Executive Director. Originally from Brooklyn, NY, she received her Master's degree in Public Administration from Strayer University. She began her AsMA employment as the Office Manager in 2006 and later became the Operations Manager. Some of Gisselle's many duties include managing the onsite registration counter at our Annual Meetings; helping new Fellows candidates with their application process; handling financial transactions for AsMA including invoices and payroll; interacting with our Certified Public Accountant; and serving as the AsMA expert on Impexium (our member database). She has also begun a doctoral program in her off-hours. As Gisselle shared, "It is a real privilege working at AsMA. I love working with my colleagues. They feel more like family! I also truly love interacting with our AsMA members from around the world."

Sheryl Kildall hails from Southern New Jersey and initially served as an analyst for a federal law enforcement agency in Washington, DC, prior to joining AsMA 24 years ago. She has served as the Subscriptions Director, interfaced with University and Military libraries, and is now the Director of Membership/Meetings. Sheryl addresses over 1500+ Annual Meeting registrations per year. She is the liaison for the AsMA Foundation, addresses membership, dues, accounts receivable, and a host of other administrative activities. Always gracious and kind, she is likely the first voice you hear answering the phone calls at AsMA to address your question or request. As Sheryl noted, "I thoroughly enjoy my work at AsMA and love putting names to faces at the annual meeting. Our members are the backbone of this organization, and we do everything possible to make being a member of AsMA an incredibly positive experience for them."

Rachel Trigg is the Managing Editor of our *Aerospace Medicine and Human Performance* journal. A New York native, she earned a Bachelor of Arts (B.A.) from Friends World College in Lloyd Harbor, NY. She also studied Library Science, earned a certificate as a Publications Specialist at The George Washington University, and a diploma from Stratford University in the culinary arts. She previously worked as a writer/editor for a number of publications, wrote restaurant and theater reviews, and served as a Proofreading Supervisor at Direct Press Modern Lithograph. She joined AsMA in 2003 as the Editorial Assistant for the journal, became Assistant Managing Editor, and now Managing Editor. Rachel edits the AsMA website, produces the monthly newsletter, assists authors during their editing and proofing process, produces the journal, and prepares the abstract submission website for the Annual Meeting. Her support of the Scientific Program Committee is vital to developing a strong program each year. Rachel noted, "It is very rewarding to pull our journal together to provide a *great read* to the membership. I am proud of our collective effort to share information across the medical and scientific communities."

Stella Sanchez joined AsMA in 2023 as the new Assistant to the Managing Editor. From Gainesville, FL, she earned B.A. degrees in Philosophy and Journalism, and a minor in Cognitive Science, from the University of North Carolina at Chapel Hill. She is currently burning the midnight oil to

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PRESIDENT'S PAGE, *continued*

earn her Master's degree in Publishing at The George Washington University. She supports authors as needed throughout the manuscript process and assists with updates to the AsMA website and newsletter. Stella shared, "I relish the opportunity to learn from the leading minds in the aerospace medicine community and contribute to the future of aerospace activities by facilitating the communication of groundbreaking research through our journal and the building of international partnerships at our meetings."

Jeff Sventek is the AsMA Executive Director, having assumed his role in 2010 as the eighth Executive Director in the history of AsMA and the first non-physician to hold that prestigious position. From the town of Sherman in Western New York State, he originally enlisted in the U.S. Air Force and subsequently completed 34 years of service, retiring with the rank of Colonel. He holds a B.S. in Biology from the University of Nebraska at Omaha and an M.S. in Physiology from Rutgers University. He is board-certified in Aerospace Physiology and is an AsMA Fellow. During his Air Force (AF) career, Jeff served as an AF Aerospace Physiologist and was the first ever Lieutenant Colonel to serve as the Chief of AF Aerospace Physiology. Jeff held numerous command and leadership positions until he retired as Deputy Command Surgeon for the Air Force Materiel Command at Wright-Patterson AFB, OH, and as 14th Chief of the AF Biomedical Sciences Corps. Following retirement, Jeff served in various government contractor positions providing human performance expertise to the Department of Defense.

As the AsMA Executive Director, Jeff serves as the Chief Operating Officer and reports directly to the AsMA Council. He guides the daily operations of AsMA and provides oversight of the current $1.6 million annual budget. Jeff also serves as the general coordinator and organizer for the Annual Scientific Meetings. During his tenure as Executive Director, Jeff has worked to modernize the Association's operations with a focus on efficiency and effectiveness. He has led AsMA through numerous management challenges during his nearly 14 years as the Executive Director: from Icelandic volcano eruptions impacting international travel, SARS, unexpected significant per diem changes, and government sequestration, to the challenges of operating a professional organization and providing educational opportunities during the COVID-19 Pandemic. Jeff has worked closely with AsMA leadership to ensure the Association remained financially protected and operationally viable. Jeff shared with me that, "my time with AsMA has truly been some of the most rewarding leadership and management experiences of my entire working career. I am always thankful that AsMA has been such a significant part of my life over decades. The international collegiality of AsMA is second to none."

As you can appreciate in the vignettes above, what a fantastic team! Hopefully you now know more about our wonderful Home Office staff and their professionalism, dedication, and commitment to AsMA.

If calling the Home Office for an issue or question, please be patient and kind and realize the staff will always work hard to get you an answer or point you in the right direction. When you see the Home Office team again at our next meeting in Chicago, whether at the Registration Desk, AsMA counter, or throughout the meeting spaces, please take a moment to share a warm smile, say hello, introduce yourself, and thank them for their service to AsMA.

I know they would greatly appreciate your kindness and good cheer… they are truly vital members of our collective AsMA family.

All the best.

Keep 'em flying…and Full Steam Ahead!

Deficient Aeronautical Decision-Making Contributions to Fatal General Aviation Accidents

Douglas D. Boyd; Mark T. Scharf

INTRODUCTION: General aviation (GA), mainly comprised of light (≤12,500 lb) aircraft, maintains an inferior safety record compared with air carriers. To improve safety, aeronautical decision-making (ADM) practices have been advocated to GA pilots since 1991. Herein, we determined the extent to which GA pilots disregard such practices.

METHODS: Fatal accidents (1991–2019) involving private pilots (PPLs) in single-engine airplanes were identified ($N = 1481$) from the National Transportation Safety Board Access[R] database. Of these, deficient go/no-go and in-flight ADM-related mishaps were scored using the PAVE (pilot, aircraft, environment, external pressure)/IMSAFE (illness, medicine, stress, alcohol, fatigue, eating) and PPP (perceive, process, perform) models, respectively. Statistical testing used Poisson distributions, Fisher exact tests, and Mann-Whitney *U*-tests.

RESULTS: Of the 1481 accidents, 846 were identified as deficient ADM-related. Electing to depart into a hazardous environment (PAVE), disregarding wellness (IMSAFE), and poor aircraft familiarity (PAVE) represented the most common categories (54%, 21%, and 20%, respectively) of errant go/no-go ADM. A 64% decline in fatal accidents related to errant go/no-go decisions for the environment category was evident over the 30-yr period, with little decrements in the other domains. Within the errant environment-related category accidents, the decision to depart into forecasted adverse weather (e.g., degraded visibility, icing, thunderstorms) constituted the most prevalent subcategory (56%, $N = 195$). Surprisingly, of this subcategory, accidents were overrepresented by over nine- and threefold for instrument-rated PPLs disregarding icing and thunderstorm forecasts, respectively.

CONCLUSION: With little decrement in ADM-related accidents in the pilot, aircraft, and external pressure domains, new strategies to address such deficiencies for PPLs are warranted.

KEYWORDS: aeronautical decision-making, general aviation, wellness, human factors.

Boyd DD, Scharf MT. *Deficient aeronautical decision-making contributions to fatal general aviation accidents*. Aerosp Med Hum Perform. 2023; 94(11):807–814.

General aviation (GA) is mostly comprised of civil, fixed-wing, single-piston engine-powered, light aircraft (≤12,500 lb)[5] engaged in nonrevenue operations. Unfortunately, this segment of civil aviation has long shown an inferior safety record in comparison with the airlines (also referred to as air carriers), as evidenced by a 60–80-fold higher accident rate.[5,24] Importantly, this difference is further amplified if only fatal mishaps are considered.[5] That said, it should be noted that for the year 2021, there was a total of 268 GA fatalities per a query of the National Transportation Safety Board (NTSB) database.[25] Several reasons likely contribute to the inferior safety for GA: 1) less stringent operational regulations[15,16] and 2) less rigorous and more infrequent pilot training/recurrency.[11] Regarding the former, for example, 14CFR 91 regulations[15] governing GA operations allow for a legal departure with zero lateral and vertical visibility. In contrast, strict weather minima must be met[16] for an aircraft, operating under the auspices of air carrier regulations (14CFR 121), to legally depart an aerodrome.

With the flexibility of GA operational regulations, and in an effort to improve safety, the aviation industry introduced the concept of sound aeronautical decision-making (ADM) to GA pilots some three decades ago.[12,13,18] By definition,[9] ADM is a

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systematic approach to the mental process used by aircraft pilots to consistently determine the best course of action in response to a given set of circumstances, be it preflight or in flight. Prior research had demonstrated that pilots who were taught this subject were safer than those aviators who did not receive such instruction.[9] From a practical perspective, preflight, a pilot weighs a variety of factors (all of which impact a flight's safety) in their decision to, or not to, initiate a flight (go/no-go decision). These include, for example: 1) the pilot's experience/currency, 2) the pilot's wellness/fatigue state, 3) aircraft capability, 4) environment viz-a-viz terrain and weather, and 5) external pressures to complete a flight.[9,18] Good ADM is equally pertinent to in-flight operations. Thus, a change in the flight situation (e.g., unforecast weather, equipment failure) will require the pilot to recognize the change and undertake appropriate measures in a timely manner to complete the flight safely.[10]

Notwithstanding the emphasis on ADM in training/recurrency over the last 30 yr, the authors are unaware of any studies to address the extent to which GA pilots have adopted (or as a corollary, disregarded) the safety practices intrinsic to such training. This gap in knowledge represents the thrust of the investigation herein. Accordingly, the specific aims of the current study were: 1) use standardized ADM schema in fatal accident analyses to identify which, if any, element(s) of the pre- and in-flight decision-making models are most frequently disregarded and 2) determine whether the rate of fatal accidents related to poor ADM has declined since introduction of the concept in 1991.

METHODS

Subjects

The research performed herein did not constitute human subject research by virtue of all data being obtained from sources/databases in the public domain.

Procedure

The National Transportation Safety Board (NTSB) aviation accident Microsoft Access® databases[25] were downloaded and queried for fatal accidents (1991–2019) occurring in the United States (excluding Alaska) involving single-piston engine airplanes (≤12,500 lb) operating under GA regulations (14CFR 91). The query was further restricted to mishaps involving aviators with a private pilot license (PPL) and for which the accident flight was undertaken for a personal mission. Instrument flight rules (IFR) rating status for PPLs and total flight experiences were determined from the NTSB accident reports. The following accidents were excluded from the study: 1) in which a second pilot was present; 2) involved a stationary aircraft; 3) for which the ownership title included entities such as LLC, LTD, Inc., Corp., or a flying club; and 4) involved homebuilt aircraft. It should be noted that querying the NTSB accident database has clear advantages over the "front-ended" web-accessible NTSB dashboard (https://www.ntsb.gov/safety/data/Pages/GeneralAviationDashboard.aspx) in that the latter does not analyze accidents prior to 2012 or allow for specific inclusion (e.g., PPLs only, IFR rating) or exclusion (e.g., second pilot, LLC, Inc., flying club) criteria as per the current study.

For the aforementioned accident cohort, those related to deficient preflight (go/no-go) ADM were identified by reviewing the corresponding final NTSB accident reports in the context of the PAVE (pilot, aircraft, environment, external pressure)[9,18] and IMSAFE (illness, medication, stress, alcohol, fatigue, eating)[9] models. For errant in-flight decision-making culminating in a fatal mishap, an adaptation of the PPP (perceive, process, perform)[10] model was employed. These schemata and their corresponding criteria are described in **Table I**. Ambiguous accidents in context of ADM were discussed and resolved by common agreement between both authors. Where departure airport weather conditions were absent from the NTSB accident report, these data were obtained from the University of Iowa ASOS network, a repository of archived weather data.[2]

ADM-related accident rates were determined using, as denominator, fleet times aggregated for the indicated period involving single-piston engine airplanes engaged in personal missions per the GA annual survey.[20] Data for 2011 were derived by interpolating 2010 and 2012 fleet times.

Statistical Analysis

A Poisson distribution[8] was used to determine if differences in fatal accidents rates were statistically significant over time. The natural log of aviation fleet time was used as an offset. Differences in proportions were tested using a Fisher exact test (two-sided).[1,21] Adjusted residuals (*Z* scores) were used to identify contributing cells. A Mann-Whitney *U*-test[21] was used to determine if differences in aviator median total flight times (h) were statistically different. All statistical testing was performed using the SPSS v27 package (IBM®, Armonk, NY).

RESULTS

A total of 1481 fatal accidents (1991–2019) involving single-piston engine airplanes operated by PPLs under the auspices of GA regulations (14CFR 91)[15] for the purpose of a personal mission were identified from the NTSB accident databases covering this period. Final NTSB reports corresponding to the aforementioned fatal accidents were manually inspected to identify those in which poor ADM was a contributing factor. Toward this end, the PAVE/IMSAFE and PPP models (Table I) for preflight (also referred to as go/no-go decision) or in-flight ADM were employed, respectively. Any accident for which a factor(s) within the PAVE/IMSAFE and/or PPP schemata was evident per the NTSB final accident report was scored as related to deficient ADM. It should be emphasized that findings in the current study are restricted to those fatal accidents related to deficient go/no-go or in-flight decisions.

Table I. Description of the ADM Models used for Fatal Accident Evaluation.

MODEL	CATEGORY	SUBCATEGORY, FACTOR, OR DESCRIPTION	ACCIDENT SCORED AS RELATED TO POOR ADM IF:
		Preflight	
PAVE	Pilot	Aviator inexperience, deficient flight recency and/or currency	One/multiple factor(s) was/were implicated in accident flight
	Aircraft	Lack of aircraft familiarity, insufficiently equipped, unable to carry planned load, incapable of operating at planned altitude, insufficient fuel for trip/leg; unairworthy	
	Environment	Adverse weather, winds, terrain (e.g., selection of inappropriate altitude), night VFR pilot in area devoid of ambient lighting	
	External pressure	"Get-there-itis", passengers, impress someone (ostentatious behavior)	
IMSAFE	I	Illness	
	M	Cognitively impairing levels of medicine, including illicit substances	
	S	Stress	
	A	Alcohol	
	F	Fatigue	
	E	Eating	
		In-Flight	
PPP		Change in flight situation (e.g., equipment malfunction, weather encounter)	Change was overlooked and/or a corrective action delayed or not undertaken

The PAVE/IMSAFE models were used to determine if an unsound go/no-go decision was made by the accident aviator. The PPP (Perceive Process Perform) schema was adapted to identify accidents relating to poor aeronautical decision-making (ADM) brought about by a changed in-flight situation which was either not recognized by the pilot or for which a corrective action was delayed or not undertaken. Equipment malfunction excludes any rendering the aircraft uncontrollable. VFR = visual flight rules.

Categorization of Deficient Go/No-Go ADM Mishaps

Using the PAVE/IMSAFE model (Table I), fatal accidents involving errant go/no-go ADM were categorized for the aforementioned 1481 fatal accidents. Interestingly, a poor preflight decision to depart into a hazardous environment (V) (e.g., adverse weather, terrain) contributed by far to the most (54%) fatal mishaps (**Fig. 1**). Fatal accidents involving pilots disregarding their impaired physical/mental well-being (e.g., illness, stress, alcohol, fatigue, cognitively impairing medicines/illicit substances) as assessed by IMSAFE (Table I) represented a smaller (21%) fraction of the fatal accidents (Fig. 1). A similar percentage (20%) of fatal accidents involved pilots who made a poor decision to initiate a flight despite a lack of familiarity with the mishap airplane (A) (e.g., equipment, flight capabilities/limitations, fuel burn). Conversely, deficiency in the pilot's flight skills in context of their experience/recency/currency (P) was evident for a smaller fraction (12%) of fatal accidents (Fig. 1). Somewhat surprisingly, flights with a fatal outcome undertaken in response to external pressure (E) represented only a modest fraction (10%) of mishaps. It should be noted that an accident may have involved multiple categories concurrently.

Sub-Categorization of Fatal Accidents Involving Errant Environment-Related Go/No-Go Decision-Making

As shown above, the majority of fatal go/no-go ADM-related accidents binned into the environment category per the PAVE/IMSAFE protocol. Since this group comprises multiple subcategories (see Table I), we then endeavored to subclassify such mishaps. Interestingly, the decision to depart into forecasted or known adverse weather represented the most prevalent subcategory (56%) of fatal accidents binned into the environment group (**Table II**). Note that adverse weather represented either: 1) any forecasted conditions cited by a Federal Aviation Administration (FAA)-approved provider in a preflight weather briefing[15] and received by the accident aviator that would be contrary to the safe completion of a flight; or 2) such weather at the departure airport at the time of departure. The preflight selection of an altitude insufficient to maintain terrain clearance or in breach of FAA regulations per low-level operations [1,000 and 500 ft (304.8 and 152.4 m) above ground level for operations over inhabited and non-inhabited areas, respectively[15]] represented the second most common group (34%) within the environment category of the PAVE/IMSAFE model.

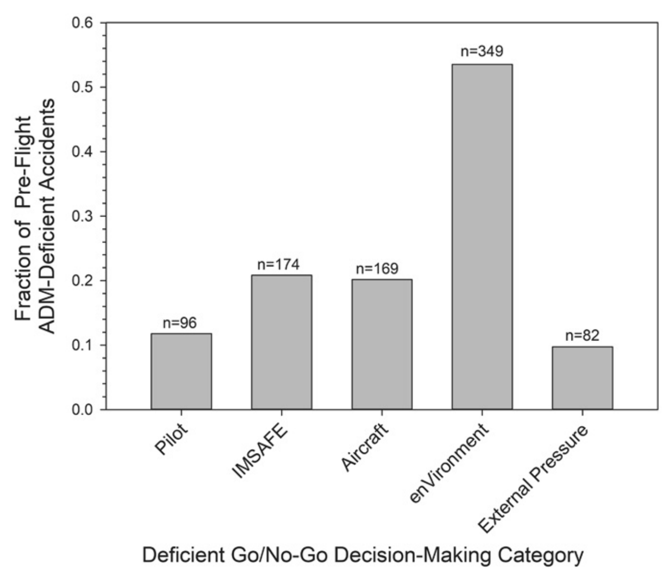

Fig. 1. Categorization of deficient go/no-go aeronautical decision-making (ADM) accidents. Fatal accidents (1991–2019) were scored for unsound preflight ADM using the PAVE/IMSAFE model per Table I. The fraction (the total representing the count of accidents related to deficient preflight ADM) of mishaps corresponding to each of the PAVE/IMSAFE categories is illustrated. Note that an accident could be scored for multiple PAVE/IMSAFE factors concurrently. *N* = accident count.

Table II. Sub-Categorization of Fatal Accidents Binned in the Environment Group.

ENVIRONMENT SUB-CATEGORY (PRE-FLIGHT ADM)	ACCIDENT FRACTION	COUNT (*N*)
Adverse Weather	0.56	195
Terrain	0.34	120
Deficient Lighting (non-IFR PPL)	0.07	23
Other	0.03	11

Mishaps related to poor go/no-go decision-making restricted to the environment category of the PAVE/IMSAFE model were subclassified per the schema in Table I. The fraction of accidents (of a total represented by the "V" category count) for each subcategory is shown. Non-IFR PPL = non-instrument-rated PPL; *N* = accident count.

The findings of "adverse weather" as the predominant subcategory of the environment group then raised the question as to the types of such weather (e.g., degraded visibility, icing or thunderstorms). It is noteworthy that adverse weather may be a function of an aviator's qualifications. By way of background, an instrument rating allows a pilot to safely conduct a flight, under the auspices of an IFR flight plan, by sole reference to instruments (e.g., in clouds, commonly referred to as instrument meteorological conditions, or IMC).[17] Conversely, in the absence of an IFR flight plan, such pilots, as well as non-IFR-rated aviators, are limited to operating using external visual references and in accordance with visual flight rules (VFR). These rules specify minima cloud-ceiling heights and lateral visibility distances.[19] On the other hand, a go/no-go decision in regards to forecasted icing and convection (thunderstorms) applies to all PPLs, regardless of IFR rating, since the majority of light aircraft are not certificated to fly in icing conditions[20] and the strong up/downdrafts associated with thunderstorms can cause structural failure of such airplanes.[23,14,34]

The decision to initiate a flight under the auspices of VFR despite forecasted weather not meeting these minima criteria was the most frequent errant preflight decision for PPLs, regardless of their IFR rating (**Fig. 2**). For the non-IFR-rated pilot, electing to depart into such hazardous conditions represented 92% of fatal accidents within the adverse weather subcategory. Note that for each pilot group (IFR rating status) accident fractions were determined using the sum of the constituent weather groups mishaps as denominator. Perhaps not surprisingly, this fraction of accidents was lower for pilots holding an instrument rating, accounting for 49% of mishaps binned into the adverse weather subcategory. Presumably these aviators, by virtue of their instrument training, are more able to maintain aircraft control upon loss of external visual cues. This difference in proportions between IFR-rated and non-IFR-rated PPLs was statistically significant ($P < 0.001$).

Interestingly though, IFR-rated PPLs were overrepresented (relative to PPLs not holding an instrument rating) for fatal accidents related to the poor decision to initiate flight into forecasted or known thunderstorms or icing (Fig. 2). Thus, the fraction of IFR-rated PPLs involved in a fatal thunderstorm encounter was threefold higher (0.15 vs 0.04, respectively) than their non-IFR-rated counterparts, a difference which was statistically significant ($P = 0.009$). Even more

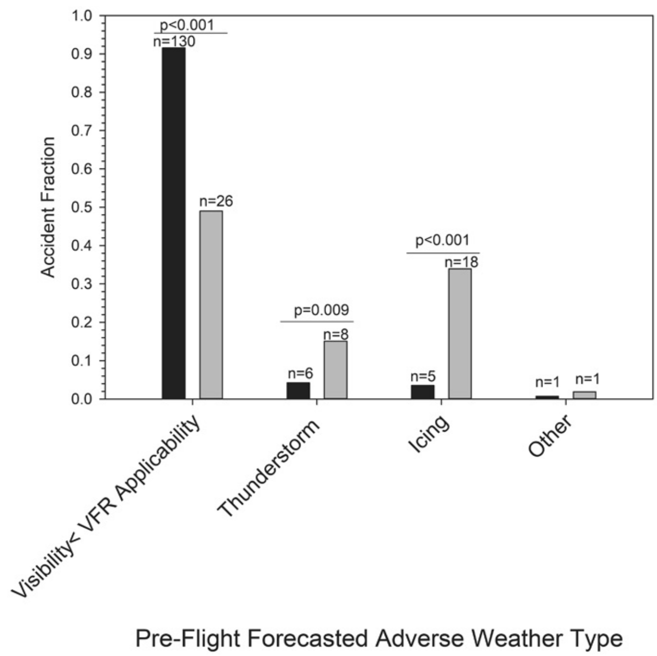

Fig. 2. Varying adverse weather types for IFR-rated and non-IFR-rated PPLs. Fatal accidents involving errant decision-making for the adverse weather subcategory (per Table II) were grouped by the indicated forecasted weather received by the aviator and whether he/she held an instrument rating. For each pilot group (non-IFR PPL = black bars; IFR-Rated PPLs = gray bars) accident fractions were determined using the sum of the constituent weather groups mishaps as denominator. "Visibility < VFR Applicability" represents forecasted cloud ceiling of <3000 ft (914.4 m)[19] for accident flights in which the pilot elected to operate by visual flight rules. Other group represents forecasted windshear and wind exceeding the maximum demonstrated crosswind limit of the accident aircraft. A Fisher Exact test (two-sided) was performed to determine if difference in proportions was statistically different. Contributions of cells were calculated from adjusted residuals (*Z* scores). *N* = accident count.

dramatic was the difference between IFR-rated and non-IFR-rated PPLs regarding their preflight decision to depart into forecasted or known icing. Again, there was a disproportionate count of IFR-rated PPLs involved in such accidents when compared to non-IFR PPLs. More specifically, for the adverse weather subcategory, while 34% of fatal accidents involved IFR-rated PPLs making the poor decision to depart into forecasted/known icing conditions, this percentage was reduced nearly tenfold for the PPLs restricted to visual flight operations. This difference was strongly statistically significant in proportion testing ($P < 0.001$).

Considering that "terrain" represented the second most common environment subcategory (see Table II) in accidents involving deficient go/no-go decision-making, we endeavored to subclassify accidents within this group. Accordingly, mishaps within this subcategory were empirically divided using the following criteria: 1) operations at low level, commonly referred to as "buzzing", i.e., flights below 500 or 1000 ft (304.8 or 152.4 m) above ground in unpopulated and populated areas, respectively, per GA regulations[15]; 2) flights for which an altitude insufficient to clear mountains/ridges was selected; and 3) low-level aerobatics performed below an altitude of 1500 ft (457.2 m)

Table III. Deficient Preflight Altitude Decision-Making.

TERRAIN	ACCIDENT COUNT (*N*)	ACCIDENT FRACTION
Low level operation/buzzing	92	0.77
Insufficient mountain/ridge clearance	11	0.09
Low level aerobatics	17	0.14
TOTAL	120	1

The fraction of fatal accidents relating to poor preflight aeronautical decision-making in context of the terrain subcategory of the environment group is shown. The sum of the accidents across constituent terrain groups represented the denominator for fraction determinations.

above ground.[15] Of particular concern, "buzzing" represented, by far, the most prevalent group (**Table III**), comprising 77% of accidents within the terrain subcategory of errant preflight ADM. In contrast, the choice of an altitude incompatible with clearing a mountainous region/ridge enroute and pilots' preflight decision to perform aerobatics at a height lower than that prescribed by FAA regulations[15] constituted only 9% and 14% of accidents, respectively, within the terrain subcategory of mishaps (Table III).

Faulty In-Flight ADM

The aforementioned data addressed accidents related to errant go/no-go ADM. However, manual inspection of the 1481 fatal mishaps occurring over the 1991–2019 period identified 296 mishaps involving unsound in-flight decision-making, using an adaptation of the PPP model[10] (see Table I). Such accidents were then subclassified using an empirical schema based on the errant ADM-related mishaps within the current cohort. Failing to recognize, or a delayed action in avoiding IMC, was by far the most common deficient in-flight decision for non-IFR-rated PPLs (77%) and IFR-rated PPLs (38%) operating under VFR (**Fig. 3**). In proportion testing, non-IFR-rated PPLs were overrepresented ($P < 0.001$) for fatal accidents in this category of deficient in-flight ADM.

Conversely, failing to recognize in-flight icing conditions or a delayed corrective response to this hazard was more likely to involve IFR-rated PPLs than aviators not certified for instrument flight (Fig. 3). More specifically, while deficient in-flight ADM applicable to icing contributed to 21% of all such fatal accidents for IFR-rated PPLs, less than 1% of mishaps could be attributed to this threat for non-IFR aviators. This difference was strongly statistically significant in proportion testing ($P < 0.001$). It is noteworthy that the same threats to flight safety were evident for accidents binned in the go/no-go ADM model (see Fig. 2).

Temporal Trends in ADM-Related Accidents

Considering the emphasis on ADM in ab initio and recurrent GA flight training since 1991,[9,12,18] the next question posed was whether the rate of fatal accidents related to deficient go/no-go ADM has diminished for each of the PAVE/IMSAFE categories over the intervening three decades. The most compelling decline in fatal accidents related to errant go/no-go decision was in the environment category, as evidenced by a 64%

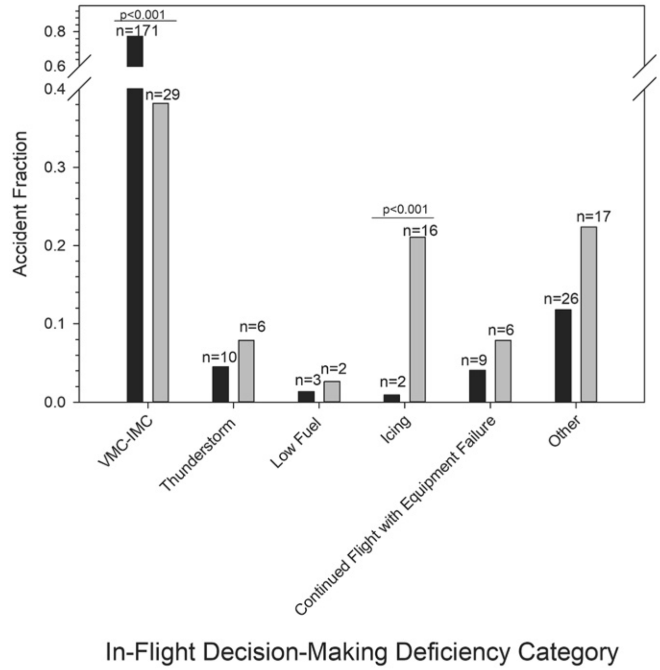

Fig. 3. Differences in errant in-flight aeronautical decision-making categories distinguish IFR-rated PPLs and non-IFR-rated PPLs. Fatal mishaps involving unsound in-flight decision-making were binned into the stated categories and by IFR-rating. Accident fractions were determined using the sum of mishaps for each pilot cohort (non-IFR PPL = black bar; IFR-rated PPLs = gray bar) as denominator. A Fisher Exact test (two-sided) was used to determine if the difference in proportions was statistically different. Contributions of cells were calculated from adjusted residuals (*Z* scores). VMC-IMC = continued flight from visual to instrument conditions; *N* = accident count.

reduction ($P < 0.001$) over the 30-yr period (**Fig. 4**). In fact, decrements in mishap rate in this category for the 2001–2005 and subsequent periods were statistically significant in a Poisson distribution ($P < 0.001$), using the initial period as referent. In contrast, reductions in the fatal accident rate related to faulty go/no-go decision making in the other PAVE/IMSAFE categories were more modest over the three decades. While improvements in go/no-go decision-making in the context of the pilot physical/mental well-being (per IMSAFE) were evident based on an accident rate reduction of up to 50% for this category for the period spanning 2006–2010, this reduction was unchanged for the most recent period ($P = 0.641$), using the initial period as referent. Regarding the pilot category, a mere 5% reduction, which was not statistically significant ($P = 0.876$), was witnessed when comparing the most recent and initial periods. Similarly, the accident rate in the preflight ADM aircraft category varied across the three decades. It diminished ($P = 0.009$) for the 2011–2015 period but not for the most recent period ($P = 0.060$), again using the initial period as referent.

Considering the prominence of deficient go/no-go ADM regarding forecasted <VFR weather, we then determined if the rate of such fatal mishaps declined over time. Indeed, this was evident with the accident rate for such accidents decreasing ($P = 0.013$) by 60% relative to the initial period (1991–1995). Presumably, aviators are making more sound decisions in the

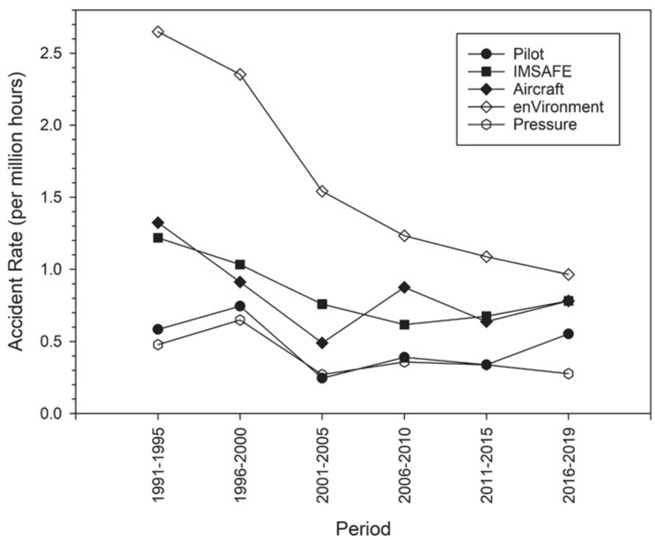

Fig. 4. Temporal changes in rates of accidents related to go/no-go deficient aeronautical decision-making. Fatal accident rates related to the indicated PAVE/IMSAFE category were determined using fleet times for single-piston engine airplanes engaged in personal missions as denominator. A Poisson distribution was employed to determine if the accident rate changed over time.

context of refraining from departing into forecasted <VFR conditions, although improvements in forecasting methodologies could be contributory.

Total Flight Experience for Aviators Involved in Accidents Related to and Un-Related to Failed ADM

Lastly, we entertained the notion that pilots with less total flight experience would be more likely to be involved in unsound ADM-related accidents than aviators who had accrued more total time. To address this question, we compared total flight times (where included in the NTSB report) for pilots involved in an accident related to deficient ADM (pre- and/or in-flight) with those in which the fatal mishap was caused by situations deemed unrelated to ADM (i.e. in-flight catastrophic equipment failure or a midair collision). While the median total flight times trended lower for aviators faulted for poor ADM (594 h and 772 h, respectively), this difference was determined not to be statistically significant using a Mann-Whitney *U*-Test ($P = 0.444$). These data do not align with the notion that inferior ADM skills correspond to lesser flight experience, although a caveat is that this conclusion is based on accident flights only.

DISCUSSION

Herein, we have shown improvements in GA safety, especially in the context of the preflight decision to initiate flights into forecast adverse weather. Notwithstanding this encouraging finding, two observations still warrant concern. First, there is a very modest (if any) decrement in go/no-go ADM in the context of the pilot, IMSAFE, and aircraft categories. Secondly, and equally important, the fraction of accidents related to errant ADM for the most recent period (2016–2019) still remains high, representing 58% of all GA accidents involving PPLs operating single-engine airplanes for the purpose of a personal mission.

Although substantial gains have been made in the go/no-go decision to initiate flight into adverse weather, this category still remains the largest for ADM-related accidents. It should be noted that this observation applied to both IFR-rated and non-IFR-rated pilots who chose to undertake a VFR flight (rather than an IFR flight) into such weather. It remains to be determined why aviators would depart into such hazardous conditions. One possibility could be the modest accuracy of the terminal aerodrome forecasts as reported in two prior studies.[6,7] In this regard, it would behoove pilots to also add the Localized Aviation MOS Program (LAMP) forecast to their preflight ADM toolkit, especially when departing aerodromes for which no Terminal Aerodrome Forecast is issued.[6] On a related note, our conservative decision to use VFR with its prescribed minimum ceiling of 3000 ft (914.4 m) above ground was based on two reasons: 1) the aforementioned poor accuracy of terminal aerodrome forecasts; and 2) the potential of man-made structures, such as antennae, reaching in excess of 2000 ft (609.6 m) AGL.

As to poor in-flight decision-making, a plethora of overlapping human factors and behavioral studies[4,36,37] have cataloged motivation type,[36,37] continuation bias,[4,26,33] and an individual's risk tolerance[27] as factors leading aviators to continue a flight[3,4] in the face of deteriorating weather (i.e., ceilings progressively lowering enroute). Unexpectedly, however, our finding of a low score (10%) of ADM-related accidents in the external pressure category of the preflight PAVE/IMSAFE model was inconsistent with this notion. We suspect though that this low fraction is due to a lower emphasis by NTSB accident investigators on capturing human factors information surrounding the accident flight.

The dramatic reduction in the rate of errant ADM-related accidents (environment category) through 2001–2005 merits comment. It is unlikely that this was due to reduced GA fleet time associated with the terrorist activities of September 11, 2001, as, by definition, the accident rate represents an adjustment for fleet activity. On the other hand, could it be that technological advancements in GA in the last 30 yr, rather than improved ADM, have yielded an artificial diminished rate of ADM accidents through 2001–2005? For example, there has been a slow but steady transition from analog flight instruments to electronic flight displays starting circa 2003.[32] Also, the introduction of the IPad[R] tablet and mobile pilot applications such as Foreflight[R] and GarminPilot[R], both compatible with this device, has allowed the aviator to identify weather hazards immediately preceding departure as well as enroute. These include, for example, thunderstorms, prevailing visibility, and cloud ceilings at enroute and destination weather-reporting airports. Thus, a potential weather-related accident could be averted, yielding an apparent lower ADM-related accident rate. However, this latter argument is improbable since the founding of the Foreflight company (2007)[22] and the introduction of the IPad[R] device (2010)[35] occurred subsequent to the improvement in ADM-related accident rate, with the latter witnessed prior to 2001–2005.

So, why then did the accident rate related to some of the go/no-go categories (pilot, aircraft, IMSAFE, external pressure) remain relatively unchanged over the 30-yr period? One possibility is the existence of a segment of the GA pilot population resistant to any notion of safety practices (and unchanged in numbers over time), instead favoring "thrill-seeking" flight activities. A second possibility is that some GA pilots are still unaware of ADM practices. Thus, while such subject matter is now integrated into ab initio flight training[18] and the WINGS program,[12] the latter activity is noncompulsory for the certified pilot. Moreover, ADM represents only a discretionary activity in mandatory flight reviews for certified GA pilots.[13] Nevertheless, whatever argument is advanced must take into account the substantial improvement in safety regarding go/no-go decision-making in context of adverse weather.

The authors recognize that faulty ADM represents a contributing rather than a causal factor for the aviation accidents herein. Still, it is well accepted[28,30] in the "Swiss cheese" model that any accident represents the contribution of multiple human failures leading to the breakdown of a complex system and, in this case, a fatal accident. Thus, had the aviator practiced sound ADM (e.g., heeding an adverse weather forecast), a fatal accident would likely have been averted.

Our current study was not without limitations. First and foremost, only deficient ADM (i.e., one which culminated in a fatal accident) could be investigated. Related to this, although the psychological (to family/friends) and financial impact of a fatal accident far exceeds that of a nonfatal mishap,[29,31] thereby rationalizing the current study, an aviator who has succumbed to his/her injuries cannot be interviewed for motivations to their ADM. Second, but equally important, we suspect the number (and hence, rate) of ADM-related accidents represents an under-count for a multitude of reasons, all related to the NTSB investigative reports: 1) earlier ones had a paucity of details on the accident flight; 2) they sometimes did not include the weather forecast or whether the accident pilot was in receipt of the corresponding hazardous conditions; and 3) they tend to focus more on regulations violated than human factor details preceding/contributing to the accident flight itself (e.g., external pressure on the aviator to complete the flight and/or mental/physical state). Indeed, it should be noted that the PAVE/IMSAFE/PPP ADM schemata are instruments developed by the FAA, whereas the NTSB has not adopted any specific instrument in their accident analysis (Dr. Loren Groff, NTSB. Personal communication; 2023). Third, we also assumed that the decision to perform low altitude operations ("buzzing", low-level aerobatics) in breach of FAA regulations was premeditated and, accordingly, binned such mishaps in the pre- rather than the in-flight decision category. Regardless, either case would represent poor ADM. Lastly, in restricting the study to the PAVE/IMSAFE and PPP models, some elements of ADM, namely hazardous attitude or antiauthority personalities, were not examined.

Finally, the findings herein raise the question: how can ADM be improved in GA? Practices recently adopted by some insurance companies for operations of light jets under 14CFR91 regulations may offer some guidance. These practices specify the requirement for a mentor pilot to be assigned and work directly with the aviator to assist in ADM practices. More specifically, new owners of turbojets require a mentor during the first 25–50 h of operating experience. In addition, such owners are also mandated to have a mentor for any flight with a family member. As another potential intervention regarding a pilot who has inadvertently encountered IMC, an air traffic controller could plainly state that "no violation will be filed" to reduce arousal associated with the fear of legal ramifications.

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Obesity and Its Relation to Excessive Daytime Sleepiness in Civilian Pilots

Radistrya Sekaranti Brahmanti; Budi Sampurna; Nurhadi Ibrahim; Nuri Purwito Adi; Minarma Siagian; Retno Asti Werdhani

INTRODUCTION: Excessive daytime sleepiness (EDS) is often associated with decreased work performance and fatigue in civil pilots. However, aeromedical recommendations for the evaluation of EDS are associated with suspicion of obstructive sleep apnea (OSA). Currently, many studies have found an association between obesity and EDS, regardless of OSA. This study aims to determine whether there is a relationship between obesity and EDS in Indonesian civilian pilots, as well as its risks for developing OSA.

METHODS: This study used a cross-sectional design and was carried out at the Directorate General Civil Aviation Medical. Subjects were asked to fill out questionnaires, including the Epworth Sleepiness Scale to measure EDS and STOP-Bang to assess OSA risk, followed by anthropometric measurements for body mass index (BMI) and waist circumference as obesity indicators.

RESULTS: A total of 156 subjects were obtained, with an EDS prevalence of 16.7%. There was no significant relationship between obesity and EDS, but the prevalence of EDS was higher in obese subjects based on waist circumference than based on BMI (17.8% vs. 15.6%). Most obese pilots with EDS had a low risk of OSA (83.3% and 80%).

CONCLUSION: The prevalence of EDS was found to be higher in pilots with central obesity compared to BMI-categorized obesity. The incidence of EDS was not correlated with the risk of OSA.

KEYWORDS: obesity, excessive daytime sleepiness.

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Daytime sleepiness is the inability to stay awake and alert during the major waking episode of the day, resulting in the person falling asleep at inappropriate times and occurring almost every day for at least 3 mo.[1] It is referred to as excessive daytime sleepiness (EDS) if it causes complaints and interferes with daily activities or functions. EDS can decrease work performance by affecting cognitive function, the information-receiving process, response time, level of alertness, and short-term memory. In the civilian pilot population, Marqueze et al. found 41.9% of Brazilian pilots have EDS and Reis et al. found 59.3% of Portuguese pilots have daytime sleepiness. EDS in the civilian pilot population is associated with sleep insufficiency due to work characteristics, excess body weight, medical history, lifestyle, and obstructive sleep apnea (OSA).[9,15]

The evaluation for EDS in civilian pilots is usually carried out when there is a suspicion of OSA. In International Civil Aviation Organization Doc 8984, Manual of Civil Aviation Medicine, if a pilot complains of snoring or a tendency to fall asleep at inappropriate times or has a body mass index (BMI) of more than $30\,\mathrm{kg} \cdot \mathrm{m}^{-2}$ and a neck circumference of more than 43 cm, an evaluation for EDS is carried out using the Epworth Sleepiness Scale (ESS). In Indonesia, based on the Ministry of Transportation Circular Number 16 Year 2018 concerning aeromedical recommendations for obesity in flight personnel with a Class 1 medical certificate, it is recommended to assess the possibility of OSA in pilots who have a BMI of more than

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35 kg · m^{-2}, along with an evaluation of sleep patterns, ESS questionnaire for EDS evaluation, and examination of abdominal and neck circumference (note if >90 cm and >43 cm, respectively).

EDS is commonly associated with obesity due to the presence of OSA. There is a sixfold increase in the risk of OSA in individuals who gain weight by 10%.[13] However, EDS can occur in obese individuals regardless of OSA, which is presumably due to a disturbance in the regulation of orexin neurons that have a role in wakefulness due to the imbalance of peripheral metabolic hormones, namely leptin and ghrelin.[12]

Obesity itself is a global health problem. In 2016, the World Health Organization noted that around 650 million people were obese. In a study conducted at Directorate General Civil Aviation Medical Indonesia in 2020, it was found that the prevalence of overweight and obese civilian pilots was 20.1% and 62.4%, respectively.[17] Given the high prevalence of obesity in civil aviation pilots, it is possible that the prevalence of EDS is also high.

A person's history of diseases such as Type 2 diabetes mellitus was also found to have a significant relationship with the incidence of EDS due to insulin resistance. In addition, EDS is also caused by decreased sleep duration influenced by a pilot's unique work characteristics, including various work schedules and flight routes that cross multiple time zones, causing circadian rhythm disturbances. Certain lifestyle choices are also associated with the incidence of EDS, such as alcohol consumption habits and physical activity.[4,5]

Based on the above, the evaluation for the presence of EDS in civilian pilots should be conducted when there is a concern about other factors besides OSA that may contribute to the incidence of EDS, especially obesity. This study aims to examine the relationship between obesity and EDS, as well as to see whether obesity influences the incidence of EDS more than other factors like work characteristics, lifestyle, and medical history.

METHODS

Subjects

This study used a cross-sectional design and was conducted at the Directorate General Civil Aviation Medical Center Indonesia from July 5–11, 2022. The study's target population was civilian pilots carrying out routine medical examinations, with inclusion criteria of being Indonesian citizens, male, ages 23–65 yr, fixed-wing aircraft pilots, and having a body mass index (BMI) of more than 18.5 kg · m^{-2}. The exclusion criteria were not filling out the questionnaire completely and medical records stating a diagnosis of obstructive sleep apnea that was confirmed through polysomnography. This study passed the ethical review of the Medical Research Ethics Committee, Faculty of Medicine, the University of Indonesia with certificate number: KET.642/UN2.F1/ETIK/PPM.00.02/2022. The subjects provided written informed consent before research participation.

Materials and Procedure

Subjects were asked to fill out a questionnaire asking about the following: age; work characteristics from the last 6 mo, including work position (captain, first officer, and single-seat pilots), amount of flight hours, frequency of night flights (occurring from 22:00–05:00), most frequent flight duration (short haul, medium haul, or long haul), and length of sleep during working days and off days; and lifestyle, including alcohol consumption and duration of exercise in the last 6 mo. To measure EDS, the Epworth Sleepiness Scale was used, which is an eight-item questionnaire that asks the subjects to determine the possibility of them dozing off in certain everyday life situations using a scale from 0–3, the highest score being the highest possibility. A score of more than 10 was considered as having EDS. As for measuring the risk of OSA, which was considered a confounding factor in this study, the STOP-Bang questionnaire was used. This is also an eight-item questionnaire, where the first four items are yes/no questions to determine whether the subjects are snoring, feeling tired, have observed apnea, or have high blood pressure. These are followed by four items that record their BMI, age, neck size, and gender. Each item is scored 1 if the subject answered yes or had a BMI of >35 kg · m^{-2}, was >50 yr of age, had a neck size >40 cm, and was male. A total score of 0–2 is determined as low risk, 3–4 as intermediate risk, and 5–8 as high risk. After filling in questionnaires, anthropometric measurements were performed for neck and waist circumference. The data for height and weight (which were measured by the health workers on duty during the medical check-up) and medical history of Type 2 diabetes mellitus (T2DM) were obtained from medical records. We classified the BMI and waist circumference based on World Health Organization—Asia-Pacific criteria, which is as follows: BMI (in kg · m^{-2}) is underweight at <18.5, normal at 18.5–22.9, overweight at 23–24.9, and obese at ≥25; central obesity for males is defined with a waist circumference of ≥90 cm.

Statistical Analysis

Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) version 22 software. Descriptive statistics of each variable were performed to assess the prevalence. Since all the variables were categorical, proportion analysis with Chi-squared or Fisher test was carried out to assess the association between the dependent and independent variables. We determined a *P*-value of <0.05 to be statistically significant. Multivariate analysis with logistic regression was then carried out to analyze the variables with a *P*-value of <0.2.

RESULTS

A total of 166 subjects participated in the study, 10 of whom were excluded because they met the exclusion criteria, hence the total sample obtained was 156 subjects. Based on age range, 71.1% of the subjects were between 23–40 yr old, with the remaining 28.3% in the age range of 40–65 yr. The prevalence of

EDS among the subjects was 16.7%. Based on BMI classification, 61.5% subjects were obese and 23.75% were overweight; based on waist circumference, 64.7% of the subjects had central obesity.

As for work characteristics in the last 6 mo, 50.6% of the subjects were first officers and the remaining were captains and single-seat pilots. The subjects' flight hours were categorized based on the median value of 200 h, where 52.6% of them had more than 200 flight hours. The subjects who had a frequency of night flights less than 10 times were 77.6%, while 10.9% had a frequency between 11–20 times and 11.5% had a frequency of more than 20 times. We found that 53.8% of subjects flew short-haul flights, followed by medium-haul, long-haul, and ultra-long-haul flights (35.9%, 9%, and 1.3%, respectively). During working and off days, the percentage of subjects who slept for more than 7 h was 55.8% and 76.9%, respectively.

As for lifestyle characteristics in the last 6 mo, 71.8% of the subjects did not consume alcohol, 23.7% consumed fewer than 5 times a month, and 4.5% consumed more than 5 times a month. The percentage of subjects who exercised for less than 150 $\text{min} \cdot \text{wk}^{-1}$ was 59.6%, while 35.9% exercised more than 150 $\text{min} \cdot \text{wk}^{-1}$ and the remaining 4.5% did not exercise at all. Many subjects had no medical history and around 8% were found to have T2DM.

For the OSA risk, 89.1% of the subjects had low risk, 10.3% of the subjects had moderate risk, and 1 subject was found with high risk.

Bivariate analysis in **Table I** showed no significant relationship between obesity and EDS, either based on BMI or waist circumference ($P > 0.05$). There was also no significant relationship between work characteristics, lifestyle, and medical history with EDS (all $P > 0.05$). Age and risk of OSA were also not found to have a significant relationship with EDS ($P > 0.05$).

Although there was no significant relationship, EDS was more commonly found in subjects with central obesity (17.8%). Meanwhile, based on BMI, the prevalence of EDS was found to be higher in subjects who were overweight (18.9%) and normal (17.4%) than in those who were obese (15.6%). However, as shown in **Table II** and **Table III**, based on the group of subjects with EDS, most of them were obese, either based on BMI (57.7%) or waist circumference (69.2%), and most had a low risk of OSA (80% and 83.3%, respectively).

When compared to the work characteristics of the subjects as shown in Table I, the prevalence of EDS is higher in single-seat pilots (25%), pilots with more than 200 h of flight (18.3%), pilots who have had night flight frequency of more than 20 times (27.8%), pilots who traveled medium-haul flights (21.4%), and pilots who slept less than 7 h on working days and off days (18.8% and 25%), all in the past 6 mo. For lifestyle, it was found that the prevalence of EDS was higher in subjects who had alcohol consumption levels less than 5 times a month (18.9%) and in subjects who did not do physical exercise (28.6%) during the last 6 mo. As for medical history, it was found that the prevalence of EDS was higher in subjects who did not have a history of illness compared to the ones with T2DM (17% and 11.1%, respectively).

Multivariate analysis was performed on the variables of night flight frequency of more than 20 times in the last 6 mo ($P = 0187$) and duration of sleep on off days for less than 7 h in the last 6 mo ($P = 0.165$), with the result that none of the variables had statistically significant values ($P > 0.05$) and inconsistent confidence intervals. The analysis also showed the Nagelkerke R^2 had a value of 0.047, indicating that the independent variables in the study had an influence of 4.7% on the prevalence of EDS.

DISCUSSION

This study found that the prevalence of EDS in Indonesian civilian pilots was 16.7%, with the highest prevalence of EDS found in the age group between 23–40 yr old. The presence of EDS can have an impact on the implementation of flying tasks as it reduces work performance by affecting cognitive function, the process of receiving information, and the level of alertness.[11] Furthermore, EDS can cause the pilot to fall asleep unintentionally, thereby increasing the likelihood of an airplane incident or accident.[9]

Although there was no significant relationship between obesity and EDS, when viewed from the group of subjects who had EDS, about 27% were overweight and almost 60% of subjects were obese. The latter findings are consistent with a study by Hayley et al.,[7] which found a significant relationship between higher BMI and EDS in the male population. Also, de Souza Palmeira et al.[4] found that sleepiness was associated with pilots who were obese. Pilots with a waist circumference of more than 90 cm in this study had a slightly higher prevalence of EDS (17.8%) than normal (14.5%), whereas in the group of subjects with EDS, almost 70% had central obesity. This is in accordance with previous studies which found an increase in the prevalence of EDS and an increase in waist circumference in the male population. There was also a significant relationship between waist circumference/central obesity and the incidence of EDS compared to BMI. The difference in the prevalence of EDS between obese subjects based on BMI and waist circumference might be because central obesity represents the distribution of abdominal visceral and subcutaneous adipose tissue. Meanwhile, BMI can be influenced by muscle mass.[6,7,10]

We did not find any significant relationship between the other factors such as age, OSA risk, work characteristics, and lifestyle which we initially thought might affect the relationship with EDS in this study. This led us to consider that it might be due to the use of a questionnaire to measure EDS, which is subjective in nature and therefore the subjects might have scored themselves higher or lower than is actually accurate. We also must consider that there could be other factors not studied in this research that are related significantly with EDS in civilian pilots.

In this study we carried out a risk assessment for OSA to see whether the incidence of EDS in obese civilian pilots was influenced by the risk of OSA. As stated previously, we did not find a significant relationship between OSA risk and EDS in this

Table I. Statistical Analysis for Obesity and Other Factors with Excessive Daytime Sleepiness.

	EXCESSIVE DAYTIME SLEEPINESS			
VARIABLES	**YES *N* (%)**	**NO *N* (%)**	***P*-VALUE**	**OR (CI 95%)**
Body Mass Index				
Obese	15 (15.6%)	81 (84.4%)	0.761†	0.88 (0.26–2.95)
Overweight	7 (18.9%)	30 (81.1%)	1.0 †	1.1 (0.29–4.3)
Normal	4 (17.4%)	19 (82.6%)	Reference	
Waist Circumference				
≥90 cm	18 (17.8%)	83 (82.8%)	0.6*	1.27 (0.52–3.15)
<90 cm	8 (14.5%)	47 (85.5%)	Reference	
OSA Risk				
High	1 (100%)	0 (0%)	0.171†	-
Intermediate	2 (12.5%)	14 (87.5%)	1.0†	0.72 (0.15–3.39)
Low	23 (16.5%)	116 (83.5%)	Reference	
Age				
23–30 yr	12 (17.9%)	55 (82.1%)	1.0†	-
31–40 yr	8 (17.8%)	37 (82.2%)	1.0†	-
41–50 yr	5 (16.7%)	25 (83.3%)	1.0†	-
51–60 yr	1 (10%)	9 (90%)	1.0†	-
61–65 yr	0 (0%)	4 (100%)	Reference	
Professional Position				
Single Pilot	1 (25%)	3 (75%)	0.53†	1.69 (0.16–17.7)
First Officer	13 (16.5%)	66 (83.5%)	0.998*	1.00 (0.42–2.36)
Captain	12 (16.4%)	61 (83.6%)	Reference	
Amount of Flight Hours				
≥200 h	15 (18.3%)	67 (81.7%)	0.566*	1.28 (0.55–3.0)
<200 h	11 (14.9%)	63 (85.1%)	Reference	
Night Flight Frequency				
>20 times	5 (27.8%)	13 (72.2%)	0.164†	2.35 (0.74–7.44)
11–20 times	4 (23.5%)	13 (76.5%)	0.294†	1.88 (0.55–6.45)
0–10 times	17 (14%)	104 (86%)	Reference	
Flight Duration				
Short haul (<3 h)	12 (14.3%)	72 (85.7%)	1.0†	-
Medium haul (3–6 h)	12 (21.4%)	44 (78.6%)	1.0†	-
Long haul (6–12 h)	2 (14.3%)	12 (85.7%)	1.0†	-
Ultra-long haul (>12 h)	0 (0%)	2 (100%)	Reference	
Sleep Duration – Workday				
<7 h	13 (18.8%)	56 (81.2%)	0.516*	1.32 (0.56–3.0)
≥7 h	13 (14.9%)	74 (85.1%)	Reference	
Sleep Duration – Day Off				
<7 h	9 (25%)	27 (75%)	0.126*	2.02 (0.81–5.02)
≥7 h	17 (14.2%)	103 (85.8%)	Reference	
Alcohol Consumption				
≥5 times/month	1 (14.3%)	6 (85.7%)	1.0†	0.87 (0.1–7,6)
<5 times/month	7 (18.9%)	30 (81.1%)	0.688*	1.21 (0.46–3.2)
Does not consume	18 (16.1%)	94 (83.9%)	Reference	
Exercise Duration				
Does not exercise	2 (28.6%)	5 (71.4%)	0.26†	2.8 (0.45–17.3)
<150 min/wk	17 (18.3%)	76 (81.7%)	0.353*	1.56 (0.6–4.0)
≥150 min/wk	7 (12.5%)	49 (87.5%)	Reference	
Medical History				
Type 2 diabetes mellitus	1 (11.1%)	8 (88.9%)	1.0f	0.61 (0.07–5.09)
No medical history	25 (17%)	122 (83%)	Reference	

*Chi-Squared; †Fisher.

population; however, it was found that the obese subjects with EDS, either based on BMI or waist circumference, mostly had a low risk of OSA (80% and 83.3%, respectively). This suggests that the incidence of EDS in obese subjects was not influenced by the high risk of OSA. Previous studies state that the pathophysiology of EDS in obese individuals is caused by an increase in leptin secretion due to increased adipose tissue in the body. When leptin receptors in the hypothalamus detect this increase, transcription of anorexigenic neuropeptides decreases, resulting in excessive sleepiness and promoting sleep fragmentation. Increased leptin is also detected by orexin receptors, which then increases inhibitory GABA neurotransmission to orexin neurons, resulting in decreased orexin signaling along with decreased physical activity and alertness. Subsequent leptin resistance decreases prepro-orexin transcription as well. In addition, in individuals with increased adipose tissue/obesity, it was

Table II. Comparison of Body Mass Index and Waist Circumference with Excessive Daytime Sleepiness.

	EXCESSIVE DAYTIME SLEEPINESS	
VARIABLES	**YES *N* (%)**	**NO *N* (%)**
Body Mass Index		
Obese	15 (57.7%)	81 (62.3%)
Overweight	7 (26.9%)	30 (23.1%)
Normal	4 (15.4%)	19 (14.6%)
Waist Circumference		
≥90 cm	18 (69.2%)	83 (63.8%)
<90 cm	8 (30.8%)	47 (36.2%)

found that there was an increase in the secretion of inflammatory cytokines such as TNF-α and IL-6, which then led to changes in the basal forebrain and anterior hypothalamus that regulate the sleep/wake cycle, increasing the intensity of non-rapid eye movement (NREM) sleep and decreasing the activity of neurons that are active in wakefulness.[2,12]

As for work characteristics, the prevalence of EDS is the highest in single-seat pilots (25%) compared to the other two professional categories. Single-seat pilots perform more tasks on short-duration flights, making them vulnerable to fatigue that can manifest as EDS.[16] The prevalence of EDS is higher in pilots who have had 200 flight hours for the past 6 mo (18.3%). Flight hours are a known contributor to fatigue in civilian pilots, where each increase in the score on the ESS questionnaire that assesses EDS has a significant relationship with the incidence of fatigue.[9,15,19] The prevalence of EDS is also found to increase in parallel with the frequency of night flying (from 14% to 27.8%). This may be due to the dysregulation of circadian rhythms influenced by night schedules. To mitigate this, a pilot is given 9 consecutive hours of rest (including sleep) within 24 h before commencing a flight duty of 9 h or less. However, various factors can affect the quality of the recommended rest time, such as sleeping environments or commuting time, hence affecting sleep duration.[9] For the flight duration frequently traveled within the past 6 mo, medium-haul flights had the highest percentage of EDS occurrences (21.4%). Fatigue occurs more often in pilots who fly short/medium-haul flights than in long-haul flights due to higher number of flight sectors, which can manifest as EDS.[14,15,19] The prevalence of EDS was highest in pilots who slept for less than 7 h on working days and off days (18.8% and 25%, respectively). Sleep restriction is one of the main causes of EDS. The American Academy of Sleep Medicine recommends a minimum of 7 h of sleep to maintain optimal health, and sleeping less than 7 h regularly is associated with decreased work performance, increased errors, and an increased likelihood of accidents.[3]

Table III. Comparison of Body Mass Index and Waist Circumference with EDS Stratified with OSA Risk.

	OBSTRUCTIVE SLEEP	EXCESSIVE DAYTIME SLEEPINESS	
VARIABLES	**APNEA RISK**	**YES *N* (%)**	**NO *N* (%)**
Body Mass Index			
Obese	High	1 (6.7%)	0 (0%)
	Intermediate	2 (13.3)	12 (14.8%)
	Low	12 (80%)	69 (85.2%)
Overweight	Intermediate	0 (0%)	2 (6.7%)
	Low	7 (100%)	28 (93.3%)
Normal	Low	4 (100%)	19 (100%)
Waist Circumference			
≥90 cm	High	1 (5.6%)	0 (0%)
	Intermediate	2 (11.1%)	13 (15.7%)
	Low	15 (83.3%)	70 (84.3%)
<90 cm	Intermediate	0 (0%)	1 (2.1%)
	Low	8 (100%)	46 (97.9%)

Then for lifestyle, the highest prevalence of EDS was found in pilots who consumed alcohol less than 5 times a month. Alcohol consumption was found to have a significant relationship with EDS.[8] There was an increase in the prevalence rate of EDS in parallel with decreased duration of physical exercise (12.5% to 28.6%). Regular physical exercise has a significant relationship with shorter sleep initiation time, shorter waking time from sleep, and longer sleep time. EEG examination also revealed a longer period of NREM stages 3 and 4 and shorter rapid eye movement sleep (REM).[18] There was also a lower prevalence of EDS in pilots with T2DM (11.1%) compared to those without a history of illness (17%). However, it is still a concern considering T2DM has been proven from other studies to be a strong independent risk factor for the incidence of EDS.[5,12] Based on multivariate analysis, work characteristics such as night flight frequency of more than 20 times and duration of sleep on off days for less than 7 h, both in the last 6 mo, were the dominant variables in this study compared to obesity.

One of the limitations of this study was the use of questionnaires, which are subjective in nature, to measure EDS. Also, based on multivariate analysis, the variables studied had a small effect on the incidence of EDS, indicating that other external factors not studied in this research contributed more than 90% to EDS in Indonesian civilian pilots. This also might explain why there were not any significant relationships between the studied variables and EDS in this study.

In conclusion, the pilots who had EDS were mostly obese and had a low risk of OSA. This highlights the importance of excess body weight management in pilots to minimize its effects on performance. However, the variables that most influenced EDS occurrence in civilian pilots are related to sleep restriction due to work characteristics rather than obesity. Therefore, besides educating the pilots regarding the incidence of EDS related to excess body weight and the impact on work performance, we also recommend for pilots to have adequate balance between working hours and resting time. Further research is recommended regarding the relation of other work characteristics outside of this study with EDS, such as length of work as a pilot, the average duration of flight duty, commuting time and vice versa, the comfort of the accommodation provided during layover, and other factors outside of work that can affect the duration of sleep, such as the home environment and social or family activities.

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Self-Reported Allergic Rhinitis Prevalence and Risk Factors in Employees of the China National Railway

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BACKGROUND: Allergic rhinitis (AR) is a common allergic disease globally and its prevalence is increasing year by year. This study aimed to analyze the prevalence and risk factors of self-reported AR among the Chinese National Railway train crew in the China Railway Beijing Group.

METHODS: This prospective questionnaire study surveyed 1511 randomly recruited train crewmembers from 20 cities in the China National Railway network, and 494 reported having AR. A structured questionnaire was tailored, designed, and delivered electronically to all subjects. Prevalence of and risk factors for AR were analyzed based on self-reported results.

RESULTS: The prevalence of self-reported AR among train crewmembers was 32.6%. Among respondents, 86.03% worked in passenger cars and 64.6% reported having worse AR symptoms while on trains. AR frequencies were 40.15% perennially and 59.85% seasonally. Among the Total Nasal Symptoms Scores (TNSS), significant differences were found between rhinorrhea and sneezing and between nasal itching and sneezing. The Rhino-Conjunctivitis Quality of Life Questionnaire (RQLQ) showed significant correlations between all seven sections. TNSS was significantly associated with the RQLQ. Scores of both the TNSS and RQLQ showed that the severity of AR symptoms ($r_p = 0.103$) and the impact on quality of life ($r_p = 0.113$) correlated significantly with seniority.

CONCLUSIONS: The prevalence of self-reported AR among train crew working in passenger cars is higher than that of the general Chinese population. The severity of AR symptoms and the impact on quality of life are associated with seniority, meaning the number of years working on trains.

KEYWORDS: allergic rhinitis, self-reported prevalence, train crew, Rhino-Conjunctivitis Quality of Life Questionnaire, Total Nasal Symptoms Scores.

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Allergic rhinitis (AR) is a noninfectious chronic inflammatory disease of the nasal mucosa mainly mediated by immunoglobulin E antibodies produced after the body is exposed to allergens. The clinical symptoms include rhinorrhea, sneezing, nasal congestion, and nasal itching.[1,18] AR is a common upper respiratory disease and is also associated with many other allergic diseases, including allergic asthma, sinusitis, eczema, dermatitis, and eye symptoms.[1] Long-term AR affects patients' moods and sleep quality, while severe AR reduces the patients' learning and working efficiency.

Epidemiological surveys have shown that the prevalence of AR has increased significantly in recent years, resulting in a larger disease burden.[16] AR is now one of the most common allergic diseases in the world. A 2013 report on allergies by the World Allergy Organization indicated that global allergic diseases have caused a huge financial and public health burden in both developed and developing countries.[13] In recent years, the rapid development of industry has resulted in serious air pollution, leading to a rapid increase in the number of people affected by AR in China.[15] In mainland China, the railway network is an important part of the national infrastructure and a

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popular means of transportation between major cities, and it plays a key role in the comprehensive transportation system. In 2019, the yearly passenger volume of the national railway reached 3.66 billion passengers in mainland China.[6] Therefore, the occupational safety and health of railway staff is related to the life and safety of passengers, which is worth noting. This study aimed to analyze the prevalence and risk factors of self-reported AR among Chinese National Railway employees.

METHODS

Subjects

This prospective survey study randomly recruited members of the train crew of the China National Railroad Beijing Group. The working positions of train crewmembers in CR Beijing include engineering, logistics, vehicle service, passenger services, and maintenance. The train crewmembers were from 20 cities in the China National Railway network. A structured questionnaire was tailored and designed and train crewmembers were randomly recruited to participate in this study to investigate the prevalence of self-reported AR by questionnaire. The study protocol was approved by the Ethics Committee of our institution. Signed informed consent was provided by all subjects prior to inclusion.

Procedure

The questionnaire consisted of two parts. The first part was the screening questionnaire, in which each subject was asked the following question: "Do you often have problems with continuous sneezing, profuse runny nose, nasal congestion or itching?" If the answer was "yes", the subject continued to answer the first specific questions in Part Two. Part Two consisted of three parts to collect the following information. 1) AR history: self-reported allergens (triggering factors); complications; history of nasal surgery; family history of allergic disease; whether the duration of nasal symptoms, perennial AR, or seasonal AR was worsened in passenger cars; and whether it correlated with working hours in the train. 2) The Total Nasal Symptoms Score (TNSS) scale included runny nose, sneezing, nasal congestion, and nasal itching. Severity of symptoms was indicated by a score from 0–4, where: 0 = asymptomatic, 1 = mild, 2 = moderate, 3 = severe, and 4 = extremely severe. 3) The Rhinitis-Conjunctivitis Quality of Life Questionnaire (RQLQ) scale included 7 sections and 28 factors. The factors affecting quality of life included these problems: activity limitation, sleep problems, performance, practical problems, nasal symptoms, eye symptoms, and emotions. A score of 0–6 indicated varying degrees of activity disturbed by nasal/ocular symptoms, where: 0 = no trouble, 1 = hardly troubled, 2 = somewhat troubled, 3 = moderately troubled, 4 = very troubled, 5 = very troubled, and 6 = extremely troubled.

AR was then diagnosed according to the criteria of Allergic Rhinitis and its Impact on Asthma guidelines. The severity and duration of AR were classified as mild, moderate/severe, intermittent, or persistent. AR was divided into perennial and seasonal AR. All subjects completed a screening questionnaire. Subjects with self-reported AR continued to complete the second part, while those without AR were automatically terminated and not included.

Statistical Analysis

Continuous data are presented as mean ± SD. Categorical data are presented as *N* (%). Differences between the four symptoms from the TNSS were measured by the Kruskal-Wallis test and the post hoc multiple comparisons by the Steel-Dwass-Critchlow-Fligner pairwise ranking nonparametric method. Additionally, Spearman rank correlation analysis was used to assess the correlations between seven sections of the RQLQ scale and the correlations between RQLQ and TNSS with the factors of seniority and worktime. All *P*-values were two-sided and $P < 0.05$ was established as statistical significance. All statistical analyses were performed using the statistical software package SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 1511 train crewmembers participated in and completed the study. Among them, 494 had self-reported AR. The overall prevalence of self-reported AR was 32.6%. The train crewmembers came from 20 cities (**Table I**). Most subjects lived in Beijing, Hebei, Tianjin, Shandong, and Shanxi. The characteristics of subjects with self-reported AR are shown in **Table II**. More than half of the subjects with AR were men (56.48%) and working in the passenger traffic section (86.03%). The mean age, seniority, history of AR, and workdays per week of the subjects with AR in this study were 33.15 ± 8.20 yr, 11.74 ± 7.93 yr, 6.32 ± 5.52 yr, and 3.64 ± 0.55 d, respectively. The most common serious symptom was nasal congestion (39.04%). A total of 67.36% of subjects thought that having AR symptoms was related to their working hours on the trains, and 64.60% reported that symptoms were exacerbated when they were on the trains. More than half of the crew with AR reported that symptoms were seasonal (59.85%) and affected their quality of life (70.63%). The common allergens were cold air (51.82%), dust mites (50.20%), and plant pollen (23.48%). The comorbidities of AR included sinusitis (20.04%), eczema (18.83%), and allergic dermatitis (12.75%). The mean TNSS was 10.20 ± 3.16, with nasal congestion (2.71 ± 0.94), rhinorrhea (2.45 ± 1.04), nasal itching (2.50 ± 0.97), and sneezing (2.54 ± 0.99). Furthermore, the RQLQ scores included activity limitation (9.68 ± 3.94), sleep problems (10.21 ± 5.02), performance (24.25 ± 11.39), practical problems (11.22 ± 5.20), nasal symptoms (14.35 ± 6.37), eye symptoms (12.8 ± 6.58), and emotions (13.06 ± 7.03). The mean RQLQ score was 94.50 ± 40.88.

The differences in symptoms from the TNSS are summarized in **Table III**. Significant differences in TNSS were found between the four symptoms (all overall $P = 0.007$). A significant difference was also noted between rhinorrhea and nasal

Table I. Geographic Distribution of Subjects' Home Cities.

CITY	COMPLETED SCREENING QUESTIONNAIRE	SELF-REPORTED AR	PREVALENCE OF AR (%)
Beijing	731	265	36
Hebei	546	167	31
Tianjin	75	25	33
Shandong	28	12	43
Shanxi	27	3	11
Guangdong	13	5	38
Shanghai	8	3	38
Jiangsu	7	2	29
Henan	7	2	29
Hunan	7	0	0
Anhui	5	2	40
Sichuan	4	3	75
Liaoning	4	0	0
Chengdu	2	2	100
Hubei	2	2	100
Inner Mongolia	1	0	0
Jilin	1	0	0
Jiangxi	1	1	100
Zhejiang	1	0	0
Missing	41	-	-

AR: allergic rhinitis.

congestion; the mean rank for all TNSS scores for rhinorrhea was higher than the mean rank for nasal congestion (mean rank: 210.22 vs. 161.30, $P = 0.016$) (Table II). **Table IV** shows significant positive correlations between the seven sections of the RQLQ scale [all Spearman's correlation coefficients (r_p) > 0.65 and $P < 0.001$], particularly the correlation between Performance and Emotions, which was extremely high ($r_p = 0.90$). Significant positive correlations were found between seniority and the TNSS or RQLQ scale ($r_p = 0.103$, $P = 0.049$; $r_p = 0.113$, $P = 0.041$, respectively), but not with working hours (**Table V**).

DISCUSSION

In recent years, the global prevalence of AR has been 10–40% and the affected individuals' quality of life was severely reduced.[2,16] AR affects 20–30% of adults in both the United States and Europe, with perhaps a somewhat higher percentage among children.[17,19] In South Korea and Japan, the incidence of AR has also increased in the past decade.[7,12] In mainland China, a multiyear longitudinal study found that the number of individuals with AR also increased year by year.[20] A questionnaire survey reported that the AR prevalence in China was 11.1% (8.7–24.1%) in 38,000 adults in 2005, but increased to 17.6% (9.8–23%) in 47,216 adults in 2011.[20] These results show that the prevalence of AR in mainland China continued to increase rapidly in the 21st century.

The present study shows that the mean prevalence of self-reported AR among the train crew was 32.6%, which is significantly higher than the national average in China. The incidence of AR among train crew living in Beijing, Hebei, Tianjin, Shandong, Shanghai, and Jiangsu was higher than the average for all train crew with self-reported AR. The high prevalence of AR in the cities where the employees live may be associated with the degree of urban industrialization, because previous studies have noted a positive correlation between the degree of urban industrialization and the severity of air pollution.[20,22]

The prevalence of self-reported AR in train crew working in passenger cars is higher than the prevalence among their colleagues in other departments (0.5–6.5%) and the general population in China (17.6%).[20] The crewmembers with AR reported that the symptoms became worse at work, while the top three antigens that trigger allergies were cold air, dust mites, and pollen. Taking train attendants' working environment and duties together, the following conditions may apply. First, the train crew usually cross through different cities, so they may experience seasonal changes and temperature alterations. Pollen during spring and autumn, and cold air during winter months, easily stimulate nasal hyperactivity.[21] Hence, the crew's AR symptoms are perennial and become worse during spring and autumn. Second, passenger cars are a special working environment with poor air circulation and high microparticle levels. The inner environment, including sponge-cushion seats, carpeted corridor, and old blankets in the sleeper, all provide suitable places for dust mites. Cha et al. investigated the concentrations of airborne particles inside trains and found that the highest exposure to PM10 and PM2.5 levels is in the passenger cars.[4] An interior ventilation system helps improve the air circulation inside trains. To attenuate the onset frequency and severity of AR among train attendants, it is critical to improve labor protections and optimize the working environment.

The present study shows that train crewmembers who are affected by AR also have comorbidities, including sinusitis, eczema, and allergic dermatitis. Prolonged severe AR has also been reported to be associated with physical and psychological symptoms, including anxiety,[8] depression, and sleep disorders.[3,9,23]

Table II. Baseline Characteristics of AR Subjects ($N = 494$).

VARIABLE	MEAN ± SD.	NO. (%)
Demographic		
Sex		
Male		279 (56.48)
Female		215 (43.52)
Age (yr) (missing = 4)	33.15 ± 8.20	
Position (missing = 14)		
Engineering		2 (0.40)
Logistics		7 (1.42)
Vehicle service		14 (2.83)
Passenger services		425 (86.03)
Maintenance		32 (6.48)
Seniority (yr) (missing = 13)	11.74 ± 7.93	
Work time (d/wk) (missing = 46)	3.64 ± 0.55	
Most serious symptoms (missing = 59)		
Sneezing		107 (24.43)
Rhinorrhea		59 (13.47)
Nasal itching		101 (23.06)
Nasal congestion		171 (39.04)
AR duration (yr) (missing = 124)	6.32 ± 5.52	
Feeling worse on trains (missing = 59)		281 (64.60)
AR related to work hours on trains (missing = 62)		291 (67.36)
History of sinus surgery (missing = 58)		20 (4.59)
Frequency of allergic rhinitis (missing = 98)		
Perennial		159 (40.15)
Seasonal		237 (59.85)
Symptom times (missing = 121)		
Symptoms 4 d/wk and 4 > consecutive weeks		188 (50.40)
Symptoms 4 < d/wk or 4 < consecutive weeks		185 (49.60)
Effect on quality of life (missing = 99)		279 (70.63)
Allergen		
Dust mite		248 (50.20)
Dog hair		24 (4.86)
Cat hair		25 (5.06)
Pollen		116 (23.48)
Cosmetics		32 (6.48)
Cold air		256 (51.82)
Unknown things on the train cars		270 (54.66)
Allergic diseases		
Asthma		22 (4.45)
Eczema		93 (18.83)
Dermatitis		63 (12.75)
Nasal polyps		31 (6.28)
Sinusitis		99 (20.04)
Without allergic diseases		237 (47.98)
Allergy history		
Parents		13 (2.63)
Father		37 (7.49)
Mother		31 (6.28)
Siblings		25 (5.06)
Child		26 (5.26)
TNSS (missing = 117)	10.20 ± 3.16	
Nasal congestion (missing = 105)	2.71 ± 0.94	
Rhinorrhea (missing = 107)	2.45 ± 1.04	
Nasal itching (missing = 96)	2.50 ± 0.97	
Sneezing (missing = 97)	2.54 ± 0.99	
RQLQ (missing = 156)	94.5 ± 40.88	
Activity limitation (missing = 116)	9.68 ± 3.94	
On train (missing = 101)	3.57 ± 1.59	
Indoors (missing = 111)	3.07 ± 1.42	
Outdoors (missing = 115)	3.10 ± 1.52	
Sleep problems (missing = 117)	10.21 ± 5.02	
Difficulty falling asleep (missing = 110)	3.40 ± 1.74	
Waking up at night (missing = 112)	3.29 ± 1.73	
Poor night sleep (missing = 111)	3.54 ± 1.82	
Performance (missing = 121)	24.25 ± 11.39	
Lack of energy (missing = 109)	3.52 ± 1.78	
Thirsty (missing = 115)	3.29 ± 1.71	
Decreased ability to work (missing = 111)	3.39 ± 1.79	
Tired (missing = 108)	3.68 ± 1.76	
Difficulty concentrating (missing = 111)	3.39 ± 1.76	
Headache (missing = 111)	3.44 ± 1.76	
Exhausted (missing = 109)	3.56 ± 1.81	
Practical problems (missing = 119)	11.22 ± 5.2	
Inconvenience of having to bring tissues (missing = 115)	3.66 ± 1.84	
Need to rub nose/eyes (missing = 113)	3.81 ± 1.77	
Need to blow your nose repeatedly (missing = 114)	3.75 ± 1.85	
Nasal symptoms (missing = 124)	14.35 ± 6.37	
Nasal congestion/stuffy nose (missing = 110)	3.97 ± 1.80	
Runny nose (missing = 118)	3.62 ± 1.81	
Sneezing (missing = 116)	3.55 ± 1.72	
Runny nose drains down throat (missing = 121)	3.27 ± 1.82	
Eye symptoms (missing = 125)	12.8 ± 6.58	
Itchy eyes (missing = 117)	3.46 ± 1.87	
Weeping (missing = 120)	3.24 ± 1.77	
Eye pain (missing = 123)	3.12 ± 1.72	
Swollen eyes (missing = 124)	3.01 ± 1.72	
Emotions (missing = 124)	13.06 ± 7.03	
Frustrated (missing = 116)	3.07 ± 1.81	
Impatient or restless (missing = 115)	3.33 ± 1.83	
Irritable (missing = 118)	3.37 ± 1.91	
Embarrassed by symptoms (missing = 119)	3.31 ± 1.84	

(continued)

AR: allergic rhinitis; TNSS: Total Nasal Symptoms Scores; RQLQ: Rhino-Conjunctivitis Quality of Life Questionnaire.

Table III. Differences in Symptoms from the TNSS ($N = 353$).

SYMPTOM GROUP	MEAN RANK	SDCF VALUE	*P*-VALUE*
A–B	193.41–210.22	1.500	0.714
A–C	193.41–166.29	2.306	0.362
A–D	193.41–161.30	3.345	0.084
B–C	210.22–166.29	3.220	0.103
B–D	210.22–161.30	4.182	**0.016**
C–D	166.29–161.30	0.397	0.992

TNSS: Total Nasal Symptoms Scores.
A: sneezing ($N = 82$); B: rhinorrhea ($N = 52$); C: nasal itching ($N = 73$); D: nasal congestion ($N = 146$); SDCF: Steel-Dwass-Critchlow-Fligner.
The overall *P*-value for comparison of TNSS levels between the symptom groups was 0.007. *P*-values < 0.05 are shown in bold.
*The Kruskal-Wallis test and Steel-Dwass-Critchlow-Fligner pairwise ranking nonparametric method was performed for the post hoc multiple comparison of the Kruskal-Wallis test.

Table IV. The Spearman's Correlation Coefficient Between Seven Sections of the RQLQ Scale.

	A	B	C	D	E	F	G
A	1						
B	0.691	1					
C	0.729	0.874	1				
D	0.746	0.753	0.824	1			
E	0.749	0.765	0.839	0.891	1		
F	0.657	0.733	0.784	0.715	0.733	1	
G	0.705	0.777	0.900	0.819	0.831	0.776	1

RQLQ: Rhino-Conjunctivitis Quality of Life Questionnaire.
A: Activity limitation ($N = 378$); B: Sleep problems ($N = 377$); C: Performance ($N = 373$); D: Practical problems ($N = 375$); E: Nasal symptoms ($N = 370$); F: Eye symptoms ($N = 369$); G: Emotions ($N = 370$).
All P-values < 0.001.

RQLQ scores in the present study also showed that problems affecting the working efficiency of train crew with AR included problems with work performance, practical problems, and sleep problems. All of these problems reduced patients' quality of life. Therefore, it is important to care for the symptoms and progress of crewmembers with AR. For example, nasal congestion caused by AR correlated positively with sleep disturbance; therefore, effective treatment for AR may improve patients' sleep quality.[23] The relationship between AR and other allergic diseases also deserves more attention, since treating one condition may also benefit the others.

AR is an allergic disease that involves a combination of genetic,[5] epigenetic, and environmental factors.[10,11,14] In the present study, ~27% of the train crew with AR had a family history of allergic disease. The prevalence of AR is comparable whether the subject's parents, siblings, or children are affected (Table II, 5–7.5%), suggesting that genetic factors play a role in AR pathogenesis. In addition, only 4.59% of the crewmembers with AR had a history of nasal surgery.

Mainland China has a vast land area, a large population, and strong population aggregation. The distance between gathering places is relatively concentrated and natural resources are unevenly distributed, so the railway has become a widely used mode of transportation in mainland China and plays a very important role in the development of the national economy.[6] The occupational safety and health of railway-related personnel has also become an important issue.

The present questionnaire survey study is limited by the relatively small sample size in Beijing city. We plan to investigate train crews of the China National Railway over the whole country and compare the prevalence of AR in different geographic areas in the future.

Table V. Spearman's Correlation Coefficient Between TNSS and RQLQ with Seniority and Worktime.

GROUP	r_p	*P*-VALUE
Total TNSS score ($N = 377$)		
Seniority ($N = 366$)	0.103	**0.049**
Worktime ($N = 345$)	−0.009	0.868
Total RQLQ score ($N = 338$)		
Seniority ($N = 329$)	0.113	**0.041**
Worktime ($N = 309$)	0.008	0.892

TNSS: Total Nasal Symptoms Scores; RQLQ: Rhino-Conjunctivitis Quality of Life Questionnaire.
P-values < 0.05 are shown in bold.

In conclusion, this is the first study focusing on the prevalence and symptoms of self-reported AR among Chinese train crew. Train attendants working in passenger cars have a high prevalence of AR, which is related to the working environment and seniority. Long-term AR also affects the mood and work performance of train crew with seniority. Through this study, we have gained a preliminary understanding of the current status and complications of AR among Chinese train crew, which may help to correct interventions to control AR in this occupational population.

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Facial Fracture Injury Criteria from Night Vision Goggle Impact

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INTRODUCTION: Military personnel extensively use night vision goggles (NVGs) in contemporary scenarios. Since NVGs may induce or increase injuries from falls or vehicular accidents, biomechanical risk assessments would aid design goal or mitigation strategy development.

METHODS: This study assesses injury risks from NVG impact on cadaver heads using impactors modeled on the PVS-14 NVG. Impacts to the zygoma and maxilla were performed at 20° or 40° angles. Risks of facial fracture, neurotrauma, and neck injury were assessed. Acoustic sensors and accelerometers assessed time of fracture and provided input variables for injury risk functions. Injuries were assessed using the Abbreviated Injury Scale (AIS); injury severity was assessed using the Rhee and Donat scales. Risk functions were developed for the input variables using censored survival analyses.

RESULTS: The effects of impact angle and bone geometry on injury characteristics were determined with loading area, axial force, energy attenuation, and stress at fracture. Probabilities of facial fracture were quantified through survival analysis and injury risk functions. These risk functions determined a 50% risk of facial bone fracture at 1148 N (axial force) at a 20° maxillary impact, 588 N at a 40° maxillary impact, and 677 N at a 20° zygomatic impact. A cumulative distribution function indicates 769 N corresponds to 50% risk of fracture overall.

DISCUSSION: Results found smaller impact areas on the maxilla are correlated with higher angles of impact increasing risk of facial fracture, neck injuries are unlikely to occur before fracture or neurotrauma, and a potential trade-off mechanism between fracture and brain injury.

KEYWORDS: night vision, maxillary fracture, zygomatic fracture, orbit injury, blunt impact.

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Head-borne night vision goggles (NVG) have become a mainstay of modern military equipment to enhance the capabilities of both aviators and ground personnel. With NVG use increasing in militaries around the world,[5] the potential risk of NVG-induced facial trauma and eye injury from falls, vehicle and aviation crashes, and other potential impact scenarios must be evaluated. The introduction of airbag systems in military rotorcraft introduces an additional source of facial trauma through impact of the airbag on NVGs being worn.[2] This study investigates the risk of injury to facial components and provides assessments of injury severity through biomechanical analysis of NVG-equivalent indenter tests on cadaveric specimens.

While most facial impact injury studies have been conducted to improve injury assessment in automobile safety or from nonlethal projectiles, this study aims to assess the risk of facial trauma from head-mounted night vision devices, an area with limited prior work. Historically since the late 1980s, Hybrid III anthropometric test dummies initially developed for automotive crash testing were used to evaluate blunt facial impacts and specifically impacts to the zygoma and maxilla in a comparison with human cadaveric heads through the use of drop towers[1,18,26] or pneumatic impactors.[16] Further modifications of the test dummy design were examined to improve

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biofidelity, including frangible faces.[25] Though a majority of these older facial impact studies are limited by the targeted application being automotive crash testing,[19] which would spread input forces over a larger area than the area of the ocular end of the NVG, and/or were directed at facial regions other than the orbits, studies have examined facial impact under smaller areas such as that of nonlethal ballistic impacts[21] using similar test methodologies. These studies are applicable for the establishment of a general range of force tolerance for skull constituents, which can act as an estimate for expected loads for NVG impacts. As these impacts also occur directly over the eyes and orbits, previous studies have also examined a potential for "blowout", a "hydraulic" or "buckling" fracture of the orbital floor through force transferred from intraorbital pressure of the globe or orbital rim, respectively,[22,23] on cadaveric human and living primate[11] models, which further complicates the potential mechanisms of fracture injuries under NVG impact conditions.

More recently, studies have focused on anthropomorphic tissue surrogates and modeling, testing through using porcine eyes[8] or a test series[3] on the Facial and Ocular CountermeasUre for Safety (FOCUS) head form developed by the U.S. Army.[4] Simulating eye injuries in cadaveric tissue with the rapid postmortem degradation of cadaveric eyes is a challenge.[12] A model with an ex-vivo porcine eye implanted inside a human orbit has been used to assess human ocular injuries since porcine eyes can be obtained immediately postmortem, before retinal detachments, and can be rapidly implanted.[6,12,24]

For facial injury assessment, though overall facial trauma has been characterized using the Abbreviated Injury Scale (AIS),[10] specific facial classifications, including Lefort[15] and Zingg,[27] describe detailed injury response in maxillary and zygomatic fractures, respectively. Donat[7] introduced a facial trauma classifier based on skeletal support mechanisms. More recently, Kunz[14] developed the AO Foundation's craniomaxillofacial (AOCMF) classification system for orbital fractures being either orbitozygomatic, nasoorbitoethmoidal, internal orbit, or combined orbit fractures involving the lateral (zygomatic) orbit wall, medial orbit wall, orbit floor, or orbital rim and internal components, respectively. The AOCMF system describes the first three fracture types as isolated, despite the possibility of overlapping, and introduces "blowout" as the injury mechanism of these three classifications in causing fracture via release of intraorbital pressure.

Global concussive head injury may be assessed with the Head Impact Criterion (HIC) for concussive head injury[20] based on the Wayne State Concussive Tolerance Curve.[17] HIC is defined as:

$$HIC = \left\{ (t_2 - t_1) \left[\frac{1}{t_2 - t_1} \int_{t_1}^{t_2} a(t)\,dt \right]^{2.5} \right\}_{max}$$

where t_1 and t_2 are the initial and final times (in seconds) of the interval during which HIC attains a maximum value; therefore, HIC includes the effect of head acceleration and duration. When the acceleration is expressed in g, an HIC value of 1000 is specified as the level for onset of severe head injury. The maximum time duration of HIC is limited to a specific value, usually 15 ms. Physically, HIC predicts that large accelerations may be tolerated for short times. HIC may be evaluated using the triaxial accelerometer at the head center of gravity.

The three principal goals of this study were to: 1) characterize NVG impact injuries to the eye and other regions using a novel method of instrumenting cadaver models, 2) elucidate loading tolerances of different regions of the orbit structure, and 3) develop region-specific quantitative risk assessments of orbital injuries from NVG impact through statistical survival analysis. NVG impact injuries were also examined in the context of the proposed and existing facial injury criteria.

METHODS

Subjects

Cadaveric testing oversight was provided by the University of Virginia Cadaver Use Committee. Physical parameters from the sectioned specimens used in this series are summarized in **Table I**. Mean specimen total body mass was 73 ± 21 kg and

Table I. Specimen Demographics and Anthropometry Summary.

	SPECIMEN							
GENERAL INFORMATION	**FRM-105**	**FRF-125**	**FRM-130**	**FF-131**	**FF-132**	**FRM-151**	**FRM-109**	**FRF-137**
Demographic								
Gender	M	F	M	F	F	M	M	F
Age at death	57	59	93	84	80	63	69	75
Mass (kg)	119	68	49	59	68	68	76	76
Stature (cm)	177.0	167.6	167.6	162.6	165.1	167.6	175.3	167.5
Anthropometry								
Head circ (cm)	56.0	54.2	54.6	53.6	53.0	61.1	53.6	52.9
Head breadth (cm)	15.0	13.5	14.4	14.0	14.0	15.0	13.5	14.2
Head depth (cm)	19.7	20.5	23.5	19.5	18.0	20.5	21.0	17.7
Head height (cm)	24.3	21.3	20.0	21.5	21.5	24.5	22.5	18.0
Head + neck mass (kg)	6.59	5.39	5.44	4.26	4.44	6.91	5.90	5.39
Potting level	T3	T4	C4	C3	C4	T4	C7	T1
Pot to O/C2 (cm)	15.0	17.2	3.5	2.0	4.5	16.0	6.0	6.5

mean stature was 169 ± 5 cm. Mean age at death was 72.5 ± 13 yr. The mean mass and stature are comparable to the 50th percentile man (70 kg, 176.8 cm). Pretest CT imaging was performed to ensure no pretest injuries.

Equipment

A pneumatic impactor and a transfer piston provided the impact. The 6.5-kg transfer piston was mounted on a low-friction mount to provide "free flight" conditions for the mass, typical of impact head/helmet mass, while limiting overall impactor stroke. High-frequency impact components were reduced using a foam decelerator mounted on the transfer piston. The impactor was calibrated to produce a piston velocity of 16 ft $\cdot$ s^{-1} (5 m $\cdot$ s^{-1}) measured by high-speed video analysis. This velocity is representative of a fall from 4.17 ft (1.27 m; i.e., less than average head height) and the input energy was ~81 J. This initial kinetic energy can be transmitted to the specimen in several ways: as strain energy in the soft and hard tissues, including fracture formation, or as kinetic energy of the specimen.

A triaxial load cell (PCB 260A, PCB Piezoelectronics, Depew, NY, United States) mounted between a simulated NVG end (US PVS-14 machined in aluminum) and the traveling mass was the primary impact assessment in axial force and shear. The positioning fixture (**Fig. 1**) used a pair of pneumatic pistons to provide adjustment in the z direction (superior–inferior). A linear bearing track, mounted across the top of two pistons, provided free motion in the x direction (anterior-posterior). A second bearing at a 90° angle to the x-axis provided free motion in the y direction (medial–lateral). An adjustable index was mounted to the lower track with x-y-z-axis rotation adjustments. A six-axis load cell (IF-210, First Technology Safety Systems, Novi, MI, United States) connected the neck potting cup to the index. All tests were recorded at 1000 frames per second using high-speed digital video. One camera (Phantom V, Vision Research, Wayne, NJ, United States) was positioned at the side of the fixture at the height of the specimen. A second camera (Kodak RO, Kodak, Rochester, NY, United States) was positioned above the fixture.

To determine the time of fracture, a pair of acoustic sensors (Nano/Pico, Physical Acoustics, Princeton Junction, NJ, United States) were glued using cyanoacrylate adhesive bilaterally to the skull. To provide a comparison with existing injury criteria, an array of accelerometers (Endevco 7270A-2K, Endevco, San Juan Capistrano, CA, United States) was mounted in the upper mandible. An additional accelerometer (Endevco 7270A-2K) was mounted on the transfer piston to measure impact mass deceleration. The instrumentation is shown in Fig. 1. Sensor output was recorded and converted to digital data by a custom high-speed data acquisition system. The data collection process was controlled with LabView software. The sample rate was 1 MHz for all channels and 64 ms of data were recorded.

Procedure

For impact, the Frankfort Plane of the specimen was aligned parallel to the local horizontal with the midsagittal plane of the specimen aligned with the x-axis. The index was adjusted about the z-axis to position the specimen for a zygoma impact or adjusted in the x-z plane for a maxilla impact. 20° and 40° impacts to the maxilla and zygoma were chosen as a reasonable range given the use case of the night vision goggle application. The fixture was then adjusted along the x-axis (anterior–posterior axis) so that the NVG profile would contact the specimen at the point in space where the transfer piston began free flight. Due to postmortem degradation of the cadaver globes and to more accurately simulate normal anatomy, the human cadaver globes were enucleated and replaced with fresh porcine globes, which were affixed by attachment of cadaver rectus muscles to the porcine globe sclera. Immediately before the test, the porcine eye was pressurized to physiological conditions by injecting the anterior chamber with saline followed by stromal hydration to prevent fluid egress. After the first test on each specimen, the untested side was palpated to ensure that fractures did not transfer from the tested side.

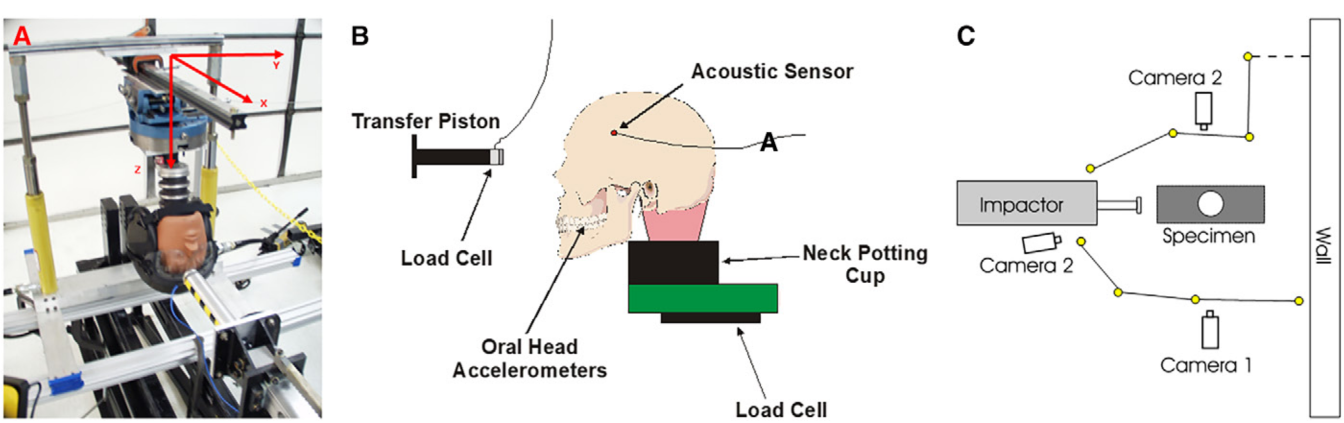

Fig. 1. A) The positioning fixture, transfer piston, and axes with placeholder Hybrid III head. B) Instrumentation overview including fixture/piston locations and specimen orientation. C) Overhead diagram of test environment.

Force/deflection characteristics were calculated using load cell data and video displacement data. Energy transferred to the specimen during the impact was calculated using video analysis. The position in space of the impacting device was determined for each video frame over the course of the event. A parametric force-deflection plot was then created using the displacement and force time histories. Then work done was found by integrating this force-displacement curve. The energy to fracture onset and the energy to the end of fracture (both as measured by the acoustic signal) were measured for the tests. The kinetic energy of the specimen was determined by integrating the acceleration signals from the nine-axis array to produce corresponding velocity time histories.

The peak velocity and specimen mass were used to find the peak kinetic energy of the specimen. To examine the impact of strain energy relative to specimen kinetic energy or fracture formation, an estimated value can be calculated with a few assumptions. For a linear elastic material, the strain energy per unit volume is given by:

$$W = \frac{\sigma\varepsilon}{2}$$

where σ represents the stress and ε represents the strain. Using Hooke's Law (σ = Eε) and multiplying by the contact area and thickness yields an equation for strain energy:

$$E_{strain} = \frac{E\varepsilon^2 At}{2}$$

where E is the elastic modulus, A is the area, and t is the skin thickness. Relative areas of impact can be ascertained by dividing energy (work done) by the force at the time of acoustic onset and squaring the result to provide a scaling measurement in terms of area that can be used to compare the different loading conditions.

To assess injury severity for zygoma impact, each of the fracture patterns was graded according to the scales used by Rhee[18] and Donat[7] The Rhee scale has the advantage of being specific to facial fracture, allowing finer distinctions to be made between similar injuries. For the Donat system, the number of buttress and beam segments that have been compromised by fracture were counted to produce a whole number score.[7]

Statistical Analysis

For this study, injury timing is assessed as the onset of fracture indicated by acoustic emission. The axial force at fracture is used as the input to the statistical models. A survival analysis based on a logistic distribution was performed on the dataset of force at acoustic onset for these tests.[13] The cumulative distribution function for the logistic distribution assumes a form of:

$$1 - \frac{1}{1 + e^{\frac{(A-F)}{B}}}$$

where F is the force in Newtons, A is the mean, and B is the "Scale" parameter. For this distribution, the mean of the dataset corresponds to a 50% risk of injury. Minitab 15 (Minitab, LLC, State College, PA, United States) was used to determine the parameter values for the data set.

RESULTS

The test matrix with impact conditions and injury assessments is shown in **Table II**. All tests except for Test 1.1 resulted in some fracture. There were few eye injuries produced in this test series; those that did occur were minor (AIS 1). Corneal abrasions resulted in Tests 1.2, 1.10, and 1.12; minor folding or shifting of the sclera occurred in Test 1.6. Representative axial force time histories for each test type are shown in **Fig. 2**.

Average peak axial force and axial force at initial fracture are shown in Fig. 2. Statistically significant differences (t-test, a = 0.05) were found for initial fracture force between the 20° and 40° zygoma impacts, and between the 40° zygoma and the 40° maxilla impacts.

All Nij values for neck injury were below the injury tolerance of 1.0 (**Table III**). To assess the influence of facial impact on neck injury level, a one-way ANOVA was performed using the Nij neck injury criterion for angle of impact and impact location with respective P-values of 0.12 and 0.05 (**Fig. 3**). This statistically significant difference in neck injury criterion between zygomatic and maxillary impacts suggests maxillary impacts are more likely to increase the risk of neck injury.

To assess head injury, calculated HIC values for the tests are shown in **Table IV**. One of the tests, NVG 1.1, resulted in a HIC value greater than 1000, indicative of potentially injurious skull/brain trauma. This test had a substantial portion of the input energy and momentum transferred to the head (68 J of kinetic energy from 81 J of input energy) but saw no fracture. The remainder of the HIC values seen in the testing were in the range of ~50–300, suggesting the risk of concussive injury from

Table II. Test Instrumentation.

MEASUREMENT	SENSOR LOCATION	AXIS	SENSOR TYPE	MANUFACTURER	MODEL
Impact force	NVG eyepiece	X, Y, Z	3-axis load cell	PCB	260A
Impactor acceleration	Transfer piston	Axial	Uniaxial accelerometer	Endevco	7270A-2K
Head acceleration	Cadaver mouth (9)	X, Y, Z	Nine axis array	Endevco	7270A-6K
Fracture detection	Left/right parietal skull (2)	N/A	Ultrasonic	Physical acoustics	Nano/Pico
Neck load, moment	Neck potting cup	X, Y, Z	6-axis load cell	First technology safety systems	IF-210

NVG: night vision goggles.

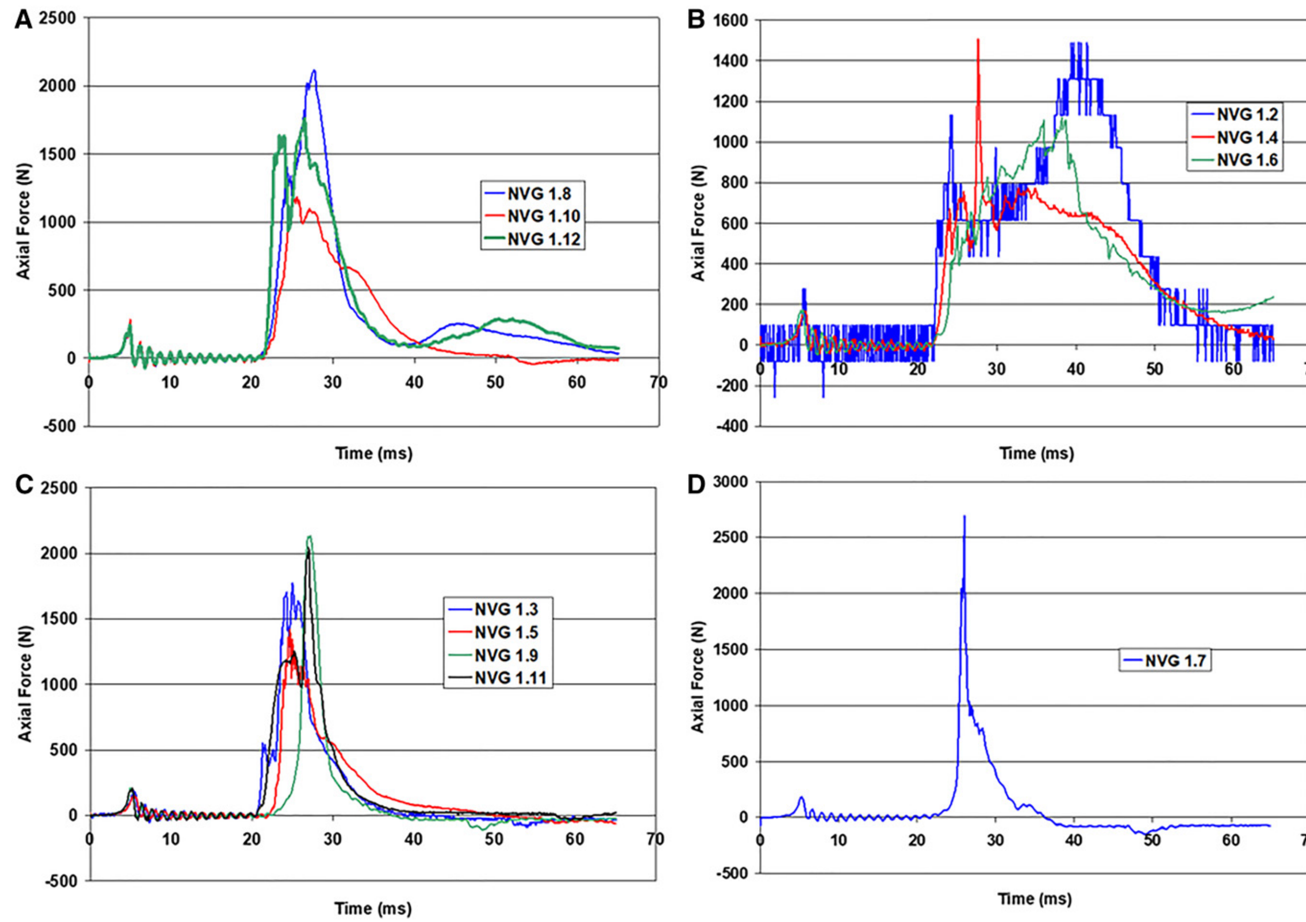

Fig. 2. Axial force time histories for: A) 20° maxilla impacts; B) 40° maxilla impacts; C) 20° zygoma impacts; and D) 40° zygoma impacts.

these impacts is low and that unmodified HIC is not a good indicator of facial fracture.

Survival analysis injury risk functions were calculated for the 20° and 40° maxilla impact scenarios and the 20° zygoma impacts (**Fig. 4**). A force of 1148 N corresponds to a 50% risk of fracture for the 20° maxilla case, 588 N for the 40° maxilla case, and 677 N for the 20° zygoma case. For the cumulative distribution function for overall survival in all impact scenarios, a force of 769 N corresponds to a 50% risk of fracture. These results with 95% confidence intervals are shown in Fig. 4.

DISCUSSION

Several parameters play key roles in characterizing injury type/severity and assessing risk due to NVG impact injuries. Of particular interest is the role facial fracture plays in reducing energy

Table III. Summary of Injury Severity.

	ORBIT INJURY SEVERITY			EYE INJURY SEVERITY					
TEST	AIS	RHEE	DONAT	INJURY	AIS	IMPACT SIDE	IMPACT LOCATION	IMPACT ANGLE	ACOUSTIC EMISSION Δt
1	0	1	0			R	zygoma	40°	12.7
2	3	6	6	corneal abrasion	1	L	maxilla	40°	23.8
3	3	5	4			R	zygoma	20°	13.2
4	3	6	5			L	maxilla	40°	13.3
5	3	6	5			R	zygoma	20°	7.9
6	3	6	6	sclera fold	1	L	maxilla	40°	18.5
7	2	2	1			R	zygoma	40°	3.5
8	3	3	3			L	maxilla	20°	5.5
9	2	2	0			R	zygoma	20°	11.1
10	3	6	6	corneal abrasion	1	L	maxilla	20°	9.5
11	3	2	1			R	zygoma	20°	11.3
12	3	5	2	corneal abrasion	1	L	maxilla	20°	9.1

AIS: Abbreviated Injury Scale; RHEE: Rhee scale—Rhee et al.[18]; DONAT: Donat et al.[7]

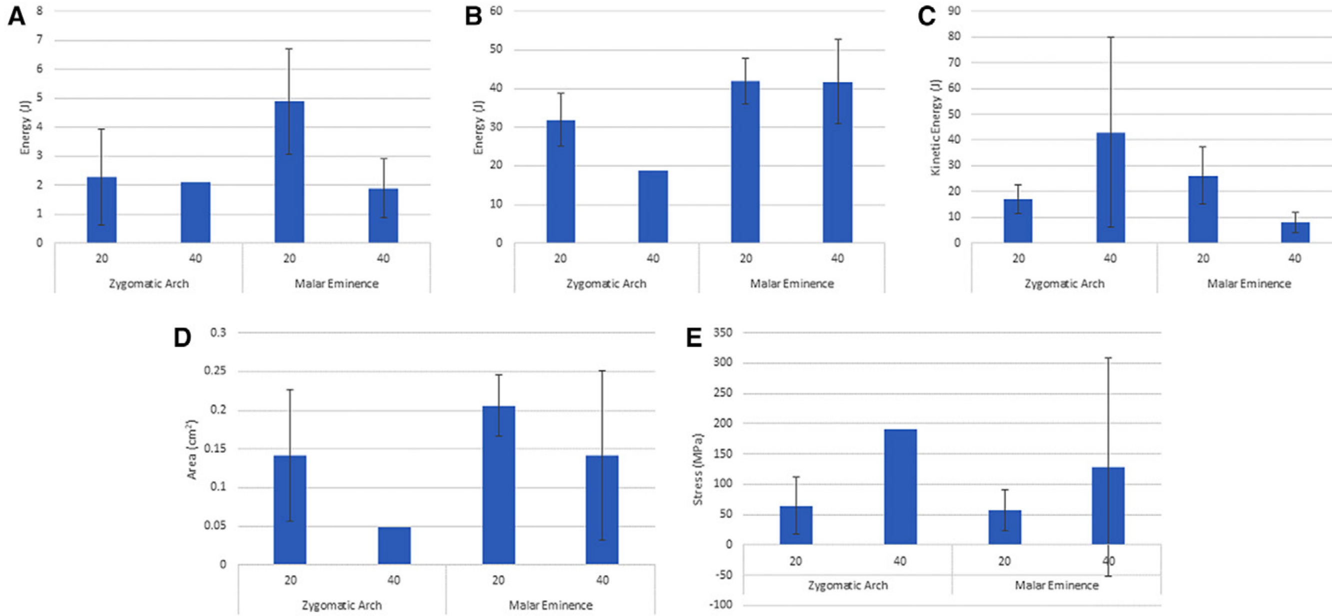

Fig. 3. Energy (± 1 SD) to: A) fracture initiation; B) end of fracture; C) peak specimen kinetic energy (± 1 SD) for the NVG series; D) area (± 1 SD) for the loading conditions; and E) stress (± 1 SD) at fracture.

transfer to further impact or injure the brain. During the one test in which facial fracture did not occur (Test 1.1), a larger fraction of the input energy was transferred to the rigid body motion of the head, producing an HIC value associated with head injury. This suggests there is a tradeoff between facial fracture and brain trauma, and that the occurrence of facial fracture may limit the risk of brain trauma. All other cases produced some degree of facial fracture with less energy transfer to rigid body motion, emphasizing the tradeoff between facial fracture and the potential of blunt neurotrauma from facial impact.

To estimate the effect of the viscoelastic properties of skin on the energy/force to fracture, Gadd[9] performed drop tests on facial skin samples at similar rates to these tests, with an elastic modulus of ~3.2 MPa with a peak strain of 0.7. Assuming a mean skin thickness of the specimens in this test series of 5 mm with NVG contact area of ~1/6 of the NVG profile area (230 mm^2), the energy storage in the skin is less than 1 J at peak strain. So, the skin energy storage is small compared with the overall input energy to the system (~79 J). Thus, the bulk of the input energy is spent either creating fractures or applying bulk kinetic energy in the specimen.

For injury severity, significant differences were found with respect to injury location and impact angle, largely from geometric effects of the underlying facial bones. Impacts to the zygoma tend to be less severe than impacts to the maxilla because the zygomatic impact is more tangential to the lateral side of the face while the maxillary impact is more normal to the front of the face. Between the 20° and 40° zygoma impacts, the 40° condition is less injurious because the NVG contacts the strong frontal bone before it reaches the zygoma. The 20° maxilla impact is generally less severe than the 40° impact because the facial bones support the more direct blow better than they do the higher angle blow,

Table IV. Summary of Measured Parameters: Axial Forces, Energy, Injury Criteria.

				AXIAL FORCES (N)			ENERGY (J)				
TEST	SPECIMEN	LOCATION	ANGLE	PEAK	ACOUSTIC ONSET	Nij	TO FRACTURE	AT PEAK FORCE	PEAK RES ACC (g)	HIC	HIC DURATION (ms)
1	FF-132	zygoma	40						223	1009	2.6
7	FRM-151	zygoma	40	2692	946	0.2	6.11	10.75	125	128	2.7
3	FRM-130	zygoma	20	1772	501	0.33	4.98	17.39	105	134	3.2
5	FF-131	zygoma	20	1421	968	0.31	7.47	10.22	85	102	5.8
9	FRF-125	zygoma	20	2133	166	0.22	4.3	14.21	104	210	3.2
11	FRM-105	zygoma	20	2015	997	0.31	9.76	32.55	138	179	6
2	FF-132	maxilla	40	1569	695	0.75			115	105	5.6
4	FRM-130	maxilla	40	1506	619	0.39	7.54	19.41	106	59	8.6
6	FF-131	maxilla	40	1119	414	0.72	6.24	39.04	82	147	15
8	FRM-151	maxilla	20	2104	1250	0.42	11.06	30.28	87	233	8.8
10	FRF-125	maxilla	20	1179	578	0.19	8.08	15.92	47	73	8.6
12	FRM-105	maxilla	20	1760	1495	0.51	10.65	26.7	166	299	5.4

HIC: Head Impact Criterion.

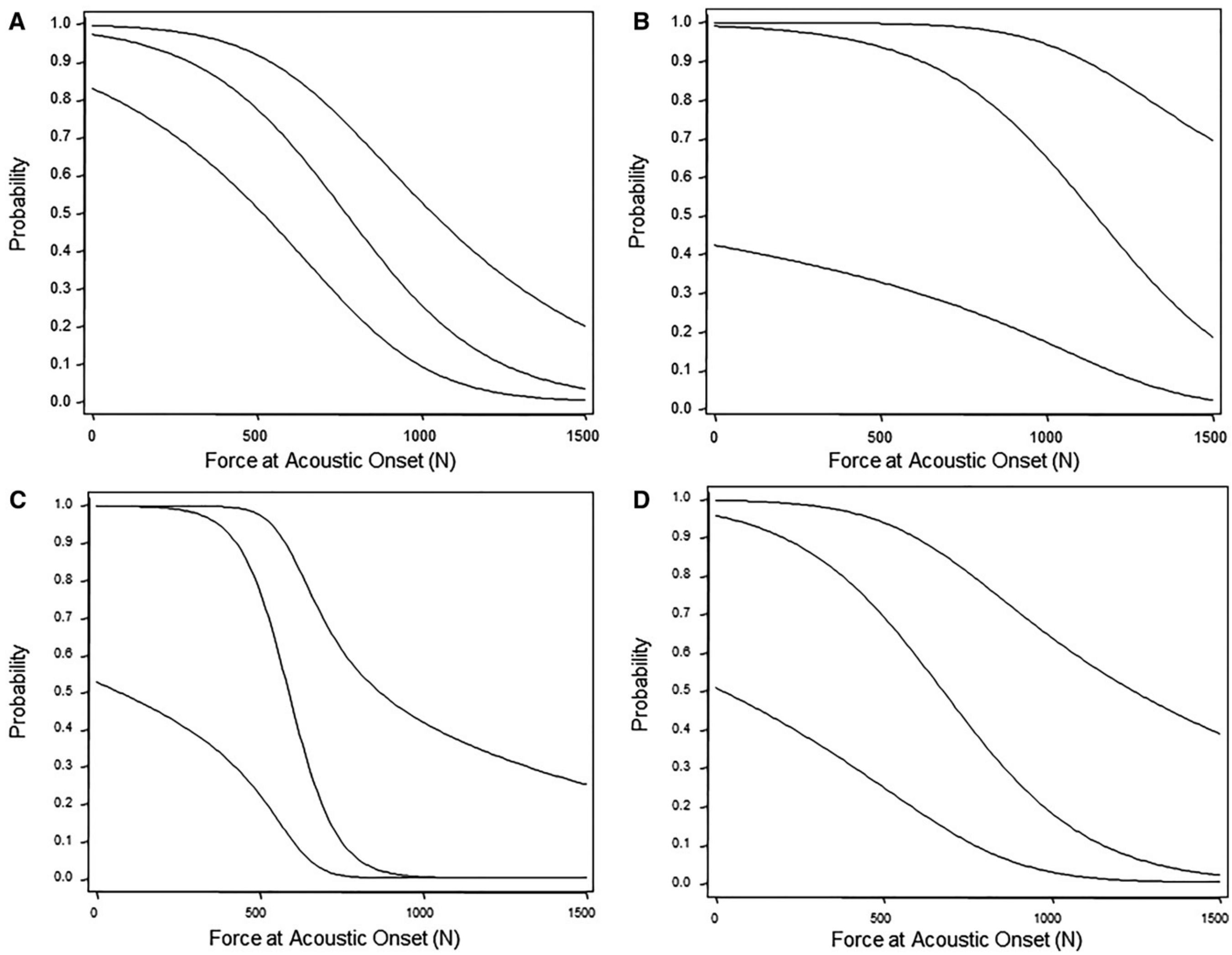

Fig. 4. Logistic survival plots for: A) all tests (50% fracture at 769 N); B) 20° maxilla case (50% fracture at 1148 N); C) 40° maxilla case (50% fracture at 588 N); and D) 20° zygoma case (50% fracture at 677 N).

which includes some shearing load. The impacts that were better supported, such as the 20° maxilla impact, require a higher energy input before the bones begin to fracture.

The survival analysis risk functions for impact peak force in this study here are consistent with previous literature.[18] Rhee found that axial forces for the zygomatic impacts range from 1359–4565 N where the current study range is 1421–2692 N with a more tightly constrained geometry. However, the peak axial force does not accurately relate to fracture tolerance of the facial bone. In addition, this study provides accurate characterization of fracture tolerances using fracture initiation identified with acoustic sensors. This use of incipient fracture formation force rather than peak force produces a realistic and accurate metric of fracture risk.

There are several important limitations in this study. Results from the porcine eye replacements showed little risk of injury to the globe beyond superficial corneal abrasions. There was little damage to the eyes from orbital floor blowout, despite the frequency of that type of injury. Since porcine eyes are generally slightly smaller than human eyes and postmortem shrinkage of orbital contents likely occurs, the model may have limited the potential for globe rupture or orbital blowout injury and resultant tissue impingement. Information about the start of crack formation provided by the acoustic sensors indicates that injury may occur at levels that are well below the peak tolerance.

In conclusion, this study used a combined cadaver-porcine head model to assess injuries to the eye and facial bones for NVG facial impact injuries. Several key factors were found to affect injury risk, including impact location, angle, axial force, and energy attenuation. Of significance are the contexts for the different injury mechanisms: facial fracture is more likely to occur with increased angle of impact at the maxilla (Fig. 4), with correspondingly lower energies for fracture initiation (Fig. 3A) owing to geometric factors, including bony support. For the zygoma, the tangential angle and influence of the frontal bone affects the injury risk. Blunt impact brain injury from NVG impact is more likely for cases without fracture, since facial fracture crack formation attenuates input energy; the nonfracture scenario transferred more kinetic energy to the head with an injurious HIC value (1009). Neck injury is impact location dependent (Table IV), but is altogether unlikely to occur before facial fracture or brain injury (all tests below the injury reference value of 1).

In this study, the tolerance of the facial bones to NVG impacts in different locations, directions, and conditions was assessed using acoustic sensors to detect the time of crack formation and injury parameters such as energy, axial force, and stress at fracture initiation. The risk of bony fracture was quantified at each impact location and for all facial fractures as a function of force with the use of statistical survival analysis. Finally, the severity of the injuries seen for the various loading conditions was assessed.

This work suggests several areas for future research. NVG-indenter testing on different models may help evaluate model fidelity, and testing models possessing midface region arrays of load cells such as the FOCUS head form may facilitate force distribution mapping. Advancements in night vision technology such as adoption of panoramic (GPNVG) or thermal fusion modules have also resulted in differences in overall NVG weights and dimensions and would necessitate further evaluation for a wider variety of impact scenarios.

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Heart Rate Variability Indices of Student Pilots Undergo Modifications During Flight Training

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INTRODUCTION: Heart rate variability (HRV) indicates the temporal fluctuation of the intervals between adjacent beats. HRV expresses neuro-cardiac activity and is generated by heart–brain interactions and dynamics related to the function of the autonomous nervous system and other components. To investigate this issue, we started a series of experiments by coupling the flight tasks of student pilots and their HRV.

METHODS: Before each experimental session, the participating student was fitted with a five-electrode, three-channel Holter electrocardiogram monitor. We defined three time-phases for each training mission: before flight operations on the ground, during flight operations, and after flight operations on the ground. The HRV analysis was performed by quantifying some indices of the time domain and the frequency domain.

RESULTS: The analysis of RR-wave intervals revealed two types of trends: 1) students whose RR intervals decreased during flight operations compared to before flight ground operations; and 2) students whose RR intervals increased during flight operations compared to before flight ground operations. These differences found in the RR intervals produced changes in the indices of both the time and frequency domains of the two students' samples.

DISCUSSION: Flight training involves regular and advanced tasks and/or emergency situations. When this happens, the total power of the heart decreases because the RR intervals are forced toward low values. Flight activity involves continuous demanding tasks that can be potentially read by an analysis of the HRV; a high HRV ensures better management of tasks that require a greater commitment of cardiovascular function.

KEYWORDS: cardiac function, heart rate variability, flight training, eustress.

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Although the heart rate is an important parameter for understanding myocardial activity levels, it is not enough for an understanding of the mechanisms underlying its modulation. For this purpose, it is much more useful to evaluate the instantaneous variation of the intervals between two consecutive R waves (RR interval) of the electrocardiogram. Therefore, the study of heart rate variability (HRV) can provide more detailed information on the modulation exerted by the autonomic nervous system (ANS) in cases where an organism leaves its resting conditions to devote itself to changing psychophysical activities. Within certain limits, this fluctuation is not a malfunction, but rather a physiological behavior given the conditions of dynamic equilibrium that distinguish the function of complex biological systems.

The HRV is therefore the result of interdependent regulatory systems that operate at different time scales on the heart. It reflects a balanced action influenced by the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS), as well as blood pressure, vascular tone, gas exchange, the intestine, and perhaps even the facial muscles.[6,9]

A stress condition implies a long-term detrimental imbalance between an individual's resources and environmental demands. From a physiological point of view, a stressful situation triggers a cascade of hormones linked to a particular

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condition, as well as an acceleration of the ANS which gives rise to muscle tension and an increase in performance.[27] Subsequently, the concept of stress has been deepened and now the scientific community prefers to speak in terms referring to the framework of the stress system. Stress is now defined as a state of homeostasis that is challenged, which includes both systemic stress and local stress. A specific stressor can elicit a specific local stress response, while stress intensity beyond a certain threshold can activate the hypothalamic-pituitary-adrenal axis and elicit a systemic stress response, also influenced by the amount of cortisol released by the adrenal cortex.[18]

The stress system includes three types: sustress (inadequate stress), eustress (good stress), and distress (bad stress). Both sustress and distress could impair normal physiological functions and even lead to pathological conditions, while eustress can benefit health through hormesis-induced optimization of homeostasis. Therefore, an optimal stress level is essential to build biological shields to ensure normal life processes. In other words, people may stress themselves unnecessarily, too much, or optimally. Stress is a form of homeostasis that is mildly challenged by moderate levels of stressors, which may induce a mild stress response, improve the buffering capacity of homeostasis, and benefit overall health.[17]

HRV can be used as a stress indicator during a sport activity,[7] to assess learning in the classroom,[8] or during a flying activity, even if only simulated.[5] The success of a learning process that occurs under conditions of extreme individual variability will depend on several concomitant factors. In pilot training, the learning process can be optimized if a flight instructor has information acquired based on the analysis of some physiological parameters of the student pilot (student). In this context, our Aviation Biophysics and Medicine Research Unit is carrying out a series of experimental procedures with the aim of quantifying the variations of some HRV indices in students who are applying to obtain a private pilot license, as well as in pilots who already hold such a license and are continuing their studies in order to acquire a commercial pilot license. Our preliminary results have been promising.[15,16] With information gained from these experimental sessions, we have made changes to the training protocol and further deepened the investigations reported above. This will allow us to obtain a sample of students as homogeneous as possible in relation to operations before, during, and after each training flight mission.

METHODS

Since the experimental protocol had to be applied to students during the flight mission, it was submitted and subsequently approved by the National Civil Aviation Authority (Aeromedical Section) of the Italian Republic.

Subjects

Participation in this project by students of both sexes took place on a voluntary basis with a guarantee of confidentiality for the purposes of processing personal data. Each subject signed the informed consent document, in accordance with the provisions of the first paragraph of Article 1 of Law 219/2017 of the Italian Republic.

Procedure

Before the experimental session and immediately after arrival, the student was equipped with five noninvasive electrodes, positioned in areas of the thoracic skin, and connected to a three-channel Holter (ECG Biomedical, BI9100) that recorded data until completion of the experimental session. The flight track (altitude, speed, track, and time) of the aircraft, obtained by using Viaair Hardware and Software[26] for the entire duration of the flight, allowed us to correlate the times at which the flight activities scheduled by the instructors took place with the Holter recordings. The training aircraft used was the Tecnam P2002JF.[23]

The training mission consisted of three phases: a ground phase that included a briefing with the flight instructor and an aircraft inspection [before ground flight operations (bfo)], an in-flight phase in which the student was asked to perform tasks scheduled by the instructor [in-flight operations (dfo)], and a ground debriefing that was scheduled at the end of the mission [postflight ground operations (afo)].

The tasks for the bfo phase were as follows: position Holter electrodes and turn Holter on; obtain weather forecast; perform mass and balance calculations; inspect airplane; briefing with flight instructor; boarding; engine starting and after-starting procedures; taxiing and aerodrome procedures; and air traffic control compliance and radio/telecommunication procedures. The tasks for the dfo phase were as follows: air traffic control compliance and radio/telecommunication procedures; straight and level flight, with speed changes, climbing (best rate of climb, climbing turns, leveling off), navigation, and maneuvers; any emergency procedures; descending; aerodrome arrival procedures; approach to landing; and air traffic control compliance and radio/telecommunication procedures. The tasks for the afo phase were as follows: engine shut down; airplane inspection; debriefing with flight instructor; and removing electrodes and turning of the Holter off.

Statistical Analysis

The HRV was quantified according to the guidelines of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).[22] We assessed the HRV data based on the time domain and frequency domain analysis.[9]

In the time domain, we quantified the mean of all RR-wave intervals and their averages before, during, and after various tasks. In the frequency domain, we quantified total power (TP) that mainly reflected the level of the autonomic nervous activities (parasympathetic and sympathetic nervous system) and high-frequency normalized units (HF, nu) versus low-frequency normalized units (LF, nu) to emphasize the balance between the sympathetic and parasympathetic arms of the ANS.

With the time domain, we computed the mean of the RR intervals (RR-int, ms), the standard deviation of all the mean normal-to-normal (NN) intervals (SDNN, ms), the square root of the mean of the sum of squares of the differences between adjacent intervals (RMSSD, ms), and the percentage of adjacent NN intervals that differed from each other by more than 50 ms (pNN50). In the frequency domain, we computed the total power (TP, ms^2), very low frequency (VLF, ms^2), low frequency (LF, ms^2), high frequency (HF, ms^2), LF normalized units and HF normalized units, and LF/HF ratio.

RESULTS

The data collected refer to a sample of 14 students of both sexes (12 men and 2 women). We report averages (±SD) of anthropometric-related factors of the subjects: age 21.64 yr (±3.13), height 1.72 m (±0.06), weight 70.93 kg (±9.57), and BMI 26.93 (±2.53). As described in Methods, we used time-domain indices to evaluate the modulation exerted by ANS, blood pressure, vascular tone, gas exchange, and hypothalamic-pituitary-adrenal axis.[18] Specifically, SDNN index is correlated with ANS activities and hormonal influences[12]; RMSSD index is a marker of parasympathetic modulation regulation of the heart;[21] and pNN50 is closely correlated with PNS activity.[24] Regarding the frequency domain, similarly to what happens in the electroencephalogram, we used this parameter to separate HRV into its VLF, LF, HF, LF, and HF normalized units, and LF/HF ratio components to describe the power spectrum density distribution.[20] The indices just described allowed us to quantify the contribution of the ANS into its sympathetic and parasympathetic components, as well as the component dependent on baroreceptor activity. An initial analysis of RR intervals revealed two types of trends: 1) nine students whose RR intervals decreased dfo compared to bfo (D-students), and 2) five students whose RR intervals increased dfo compared to bfo (I-students).

Fig. 1 (histograms A–D) depicts time-domain analyses of the two samples of students. Averages of RR intervals, SDNNs, RMSSDs, and pNN50s of both D-students (white columns) and I-students (gray columns) are shown, with dfo compared to bfo. In both samples, afo values are also reported to determine recovery. Panel A shows RR interval averages of D-students (dfo = 597.59 ms ± 35.36 compared to bfo = 675.00 ms ± 75.28) and I-students (dfo = 599.69 ms ± 33.85 compared to bfo = 551.63 ms ± 44.66). Panel B shows SDNN averages of D-students (dfo = 37.34 ms ± 35.36 compared to bfo = 52.65 ms ± 75.28) and I-students (dfo = 41.58 ms ± 10.38 compared to bfo = 42.48 ms ± 16.11). Panel C shows RMSSDs of D-students (dfo = 25.56 ms ± 09.00 compared to bfo = 34.36 ms ± 15.51) and I-students (dfo = 28.56 ms ± 10.12 compared to bfo = 28.75 ms ± 13.91). Panel D shows pNN50s of D-students (dfo = 04.11 ms ± 03.99 compared to bfo = 07.86 ms ± 05.98) and I-students (dfo = 08.05 ms ± 04.12 compared to bfo = 06.60 ms ± 06.02). Panel E shows percentage changes of RR intervals, SDNNs, RMSSDs, and pNN50s dfo in the two samples (D-students and I-students).

Fig. 2 depicts the frequency-domain analyses of the two samples of students. The left column histograms (A–D) show data of D-students dfo compared to bfo. Afo average values are also reported for recovery estimation. Panel A is box and whisker plots of total power averages; a decrease of 46.56% was observed dfo (969 ms^2 ± 540.74) compared to bfo (1814.19 ms^2 ± 1064.52). Panel B is a histogram of VLF, LF, and HF averages showing a decrease of all frequency values dfo. Panel C's histogram depicts data reported in Histogram B, calculated as a percentage to compare the magnitude of each frequency. As can be seen in the bfo column, the largest component is represented by LFs (55.13%), followed by VLFs (28.14%) and HFs (16.73%). All frequency bands dfo undergo a decrease that is more marked for HFs [7.99% (-52.25%)], followed by VLFs [14.95% (-46.88%)] and LFs [31.39% (-43.05%)]. In Panel D, in order to magnify the balance between sympathetic and parasympathetic arms of the ANS, we computed both LFs and HFs as normalized units. Values are reported as insets.

The right column histograms (E–H) show data of I-students dfo compared to bfo. Afo averages are also reported for recovery estimation. In Panel E, box and whisker plots show total power averages; an increase of 8.30% was observed dfo (1272.04 ms^2 ± 555.27) compared to bfo (1174.60 ms^2 ± 791.09). In Panel F, histograms of VLF, LF, and HF averages show a more complex trend: an increase of LFs and HFs, and a decrease of VLFs. In Panel G, the histogram depicts data reported in Histogram F, calculated as a percentage to compare the magnitude of each frequency. As can be seen in the bfo column, the largest component is represented by LFs (34.26%), followed by VLFs (16.90%) and HFs (13.58%). VLFs only undergo a decrease [14.37% (−14.98%)] dfo, while an increase was observed for HFs [16.76% (+23.40%)] and LFs [34.26% (+13.79%)]. In Panel H, in order to magnify the balance between sympathetic and parasympathetic arms of the ANS, we computed both LFs and HFs as normalized units. Values are reported as insets. The histogram at the bottom left summarizes data related to the ratio of LFs to HFs average values related to both D-students and I-students. Finally, the histogram at the bottom right contains the same data related to LFs/HFs but calculated as percent variation dfo. Note the increasing trend of the ratio in D-student dfo.

DISCUSSION

It is well known that the heart is an electromechanical pump that propels oxygenated blood in proportion to demand and receives deoxygenated blood from the whole body,[11] and that this activity depends upon the myocardiocytes of the heart (Frank-Starling Law). The heart's function can be influenced by age, lifestyle, physical activity, lack of exercise, metabolic disorders, nutritional status, physiological changes, pathological conditions, and so on.[4] The heart works actively, constantly, and is influenced by areas of the brain, both directly and indirectly.[25] During the first studies of this topic, Hans Selye[19] defined stress as the nonspecific response of the body to any request for change.

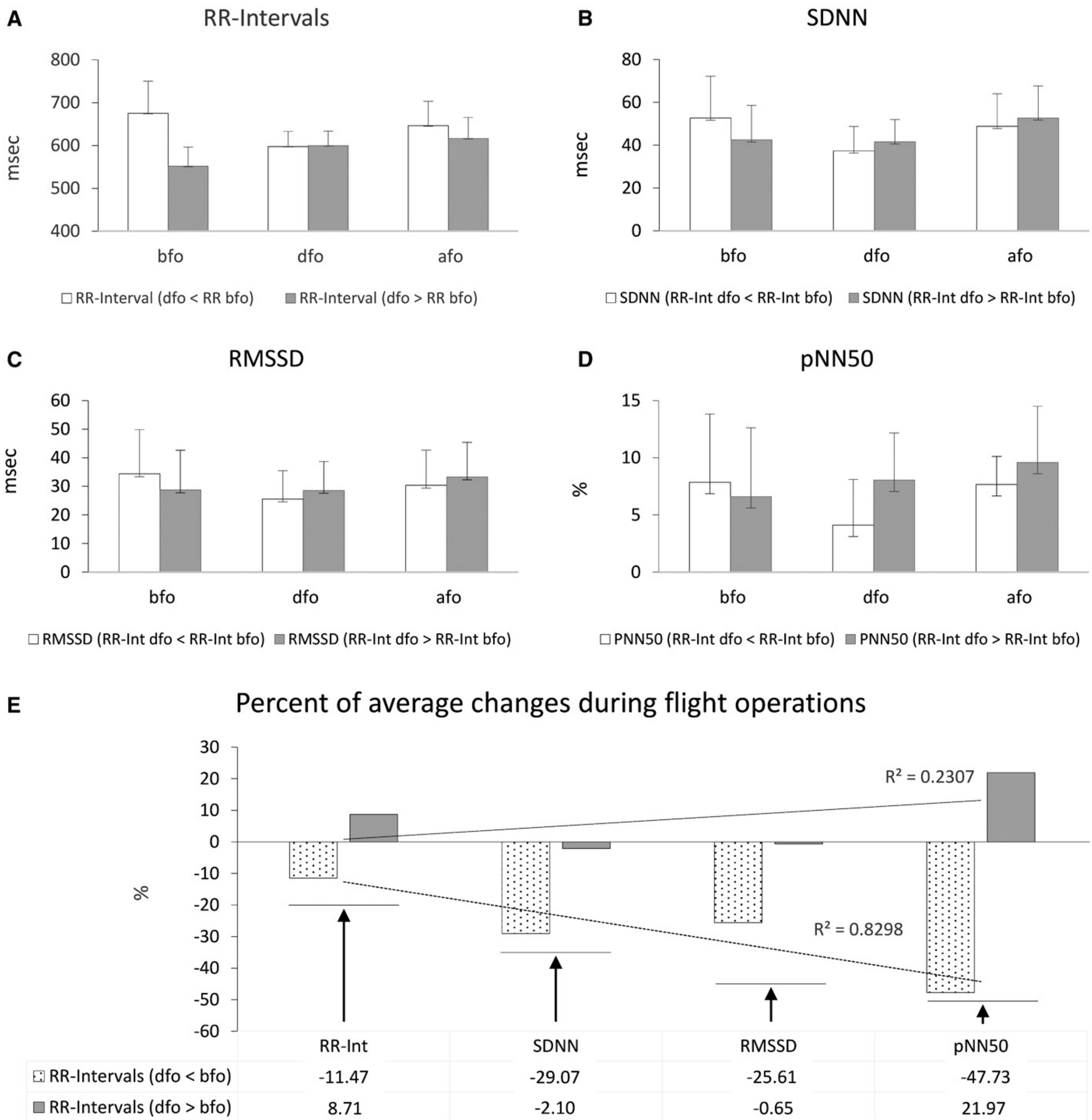

Fig. 1. Time-domain analysis (average indices). White columns refer to D-students; gray columns refer to I-students. A) RR intervals; B) SDNNs; C) RMSSDs; D) pNN50s; E) percentages of RR intervals, SDNNs, RMSSDs, and pNN50 during flight operations of both D-students and I-students computed as percent of changes. Error bars: SD.

HRV is a commonly used indicator of ANS activity that is strictly linked to alert/stress conditions and stress scenarios. In our case, the quantification of its indices (time domain and frequency domain) has given us the opportunity to gain a deeper understanding of some aspects concerning the flight training of students at their first approach to an airplane. In this regard, we report that all the student pilots participating in the research had never had any flight experience before, had been informed in advance about the aims of the research, and were advised that participation was on a voluntary basis covered by privacy. In particular, this study has also allowed us to extrapolate information about a) the human–machine relationship and b) any changes that could improve the flight training process.

A learning process, whether theoretical or practical, presupposes a commitment of various components of the nervous system, as well as other organs and systems, that can achieve

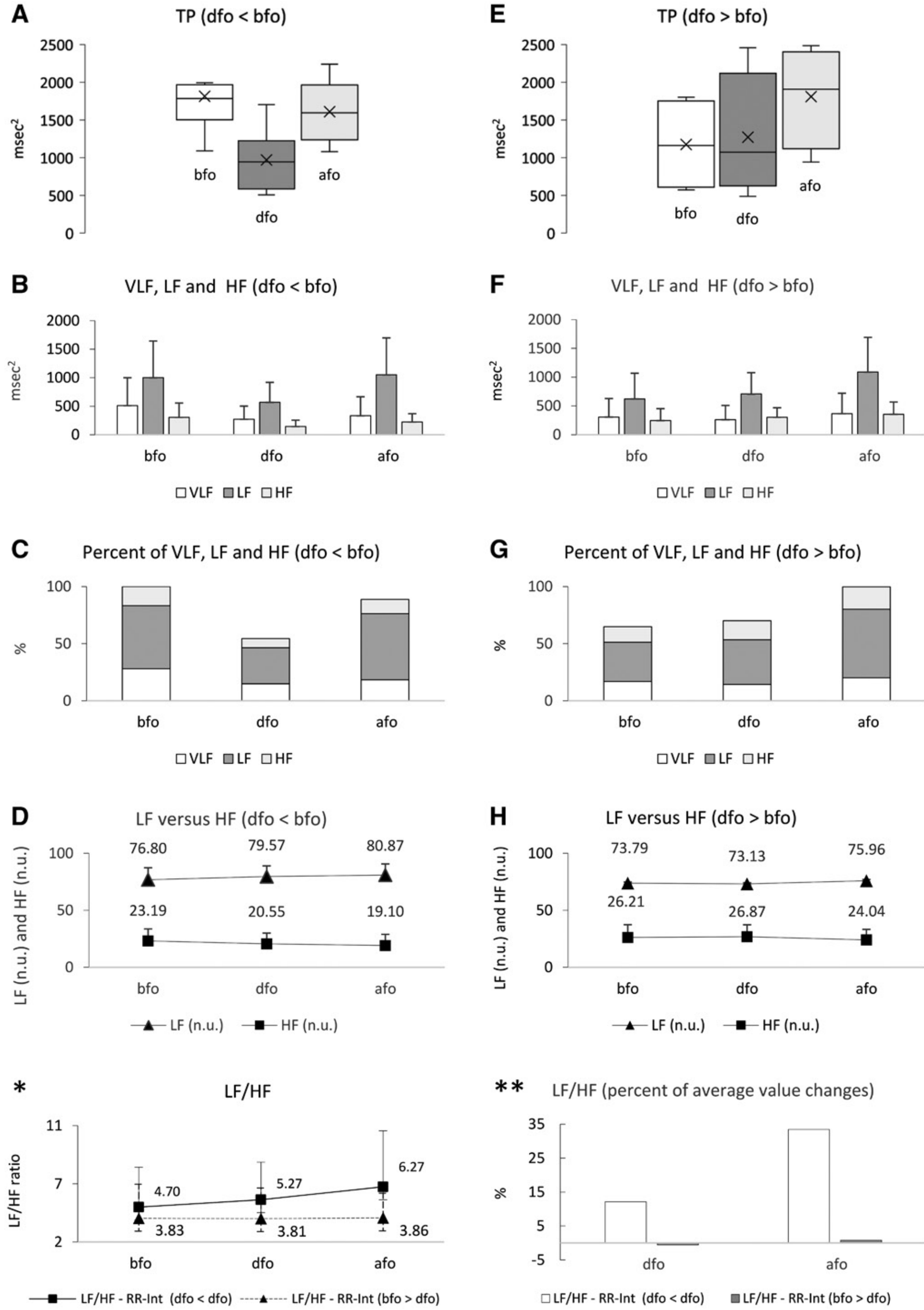

Fig. 2. Frequency-domain analysis (average indices). Left column (histograms from A–D): data related to D-students. A) Box and whisker plots of total power averages. White box bfo, heavy gray box dfo, light gray box afo. B) Histogram of VLF (white columns), LF (heavy gray columns), and HF (light gray columns) bfo, dfo, and afo. C) Same data reported in B but calculated as a percentage to compare the magnitude of each frequency. D) LF versus HF normalized units. Values are reported as insets. Right column (histograms from E to H): data related to I-students, dfo compared to bfo. E) Box and whisker plots of total power averages. White box bfo, heavy gray box dfo, light gray box afo. F) Histogram of VLF (white columns), LF (heavy gray columns), and HF (light gray columns) bfo, dfo and afo. G) Same data reported in F but calculated as a percentage to compare the magnitude of each frequency. H) LF versus HF normalized units. Values are reported as insets. *Ratio of LFs to HFs averages. Black squares show LFs/HFs ratio of D-students, whereas black triangles show LFs/HFs ratio of I-students. **LFs/HFs of averages changes dfo and afo compared to bfo. White columns report LFs/HFs ratio of D-students, while gray columns show LFs/HFs ratio of I-students. Error bars: SD.

the final goal: learning a concept, scenario, sound, etc,. or an action/task. Leaving aside the concepts of flight theory, and assuming that the students have already acquired the necessary knowledge, we will deal with what is needed to fly an airplane. Familiarization with the airplane and its flight controls is an essential prerequisite. Therefore, all motor acts foreseen for a given maneuver (e.g., a takeoff, a climbing turn, or a slow flight) must be acquired, planned, implemented, verified, corrected, and improved on the basis of what was learnt during the classroom lessons. All this will take place in a mental context originating from the character and personality of the student and his/her attraction for flight. Finally, it is important to note that flight operations take place in a three-dimensional environment in which weather conditions play an important role.

As mentioned above, HRV can be assessed with various analytical approaches, although the most commonly used are frequency domain, power spectral density, and time-domain analysis. Time-domain indices of HRV quantify the variability of the interbeat interval, which is the time period between successive heart beats,[20] hence the first indications, according to which some students face alert conditions dfo, while others are already alerted in the preliminary phases bfo. This alert/stress condition would be expressed by the decrease of the RR interval values.

The histogram shown in Fig. 1E compares the trend of the indices relating to the RR intervals, SDNNs, RMSSDs, and pNN50s in the two samples of students, and the columns indicate the percentage variation of the indices. The literature on this topic[20,21] indicates that the SDNN index refers to the activity of the ANS as a whole, while RMSSD and pNN50 indices are mainly correlated with the parasympathetic branch of the ANS. One can see that the magnitude of the indices is more marked in D-students dfo (see R^2 values in both cases). The maximum variation is reached by the pNN50 index, whose sharp decrease expresses a consistent decrease in HRV. In the opposite case with I-students, the recovery is more moderate. The data suggest an unbalanced management of HRV, which can be interpreted as a condition in which PNS and SNS would have different specific weights.

Table I shows the numerical data relating to the graphs of Fig. 1 (A, B, C, D). Note that the values of the RR intervals of both samples of students dfo are almost identical (values in bold with an asterisk), while they are quite different bfo and afo. Indeed, they are greater in one case and less in the other. This leads us to assume that HRV has its own standard dfo, i.e., that an already evident alert status condition bfo expresses lower HRV values than dfo, while higher HRV conditions bfo express a higher alert status (HRV decrease) dfo. Now, we can imagine the RR intervals dfo values of both samples of students as expressing eustress, just as the values found afo (>dfo) indicate an increase in HRV. Furthermore, data depicted in Histogram E of Fig. 1 supports the idea that HRV is quantitatively more controlled by the PNS than that exercised by the SNS, since the percentage variations of the different indices in the two samples are not superimposable. Finally, the values of the RR intervals, in one case higher than those found dfo, and in the other case lower than those found dfo, indicate that some students exhibit normal operating conditions in the bfo, while others could already be in conditions of eustress caused by situations not included in the bfo and/or caused by the bfo.

Frequency-domain indices estimate the power distribution as a function of frequency bands.[5,20] Box and whisker plots A and E of Fig. 2 depict the total power (TP) of the two samples of students; note that TP averages of D-students bfo (1814.19 ms^2) is almost equal to that of I-students afo (1809.95 ms^2). The data observed on TP in both samples of students lead to a preliminary conclusion. It is possible to identify a common (and maximum) mean value of TP bfo in D-students. Conversely, it is possible to observe the same value afo in I-students dfo. In this case, a greater size of the boxes is also observed, reflecting a greater dispersion (variability) of the TP, perhaps generated by a sustress or distress that starts to become eustress. More generally, we could imagine a system stress, as described by Lu.[17]

Histograms C and G of the same figure depict, in both samples of students, the contribution of VLFs, LFs, and HFs which, as it is known, operate within different frequency ranges. A datum common in both cases is the conspicuous presence of LFs bfo, dfo, and afo. Considering data of D-students dfo, the three frequency bands also decreased dfo, to recover afo, even if not entirely (Histogram C). Conversely, in I-students, LFs and HFs increased, while VLFs did not. Finally, the recovery was total afo (Histogram G). The literature in this regard[13,20,22] associates the aforementioned frequency bands with various components that refer to the effects exerted by branches of the ANS, the aortic and carotid baroreceptors, the pressure regulated by baroreceptive reflexes, and reflexes related to the respiratory cycle.

As mentioned above, in both samples of students there is a conspicuous presence of LFs (0.04–0.15 Hz) bfo, dfo, and afo. LF power can be produced by both SNS and PNS[3,14,22] as well as blood pressure regulation via baroceptors,[10] primarily by the PNS. LFs decrease in D-students dfo.

Bearing in mind that the HFs or respiratory band (0.15–0.4 Hz) is primarily produced by the PNS and is highly correlated with the pNN50 and RMSSD indices,[13] it is reasonable to observe its almost halving in the sample of D-students dfo. In other words, the HRV would be proportional to the parasympathetic input. For this reason, it would be reasonable to observe an increase, albeit modest, of HFs in I-students. The trend of the VLF band (0.0033–0.04 Hz) was more complex. The intracardiac nervous system is involved in the genesis of the VLF rhythm, and, furthermore, the SNS influences the amplitude and frequency of its oscillations.[21] In addition to

Table I. RR Intervals, SDNN, RMSSD, and pNN50 Averages.

	LOWER RR INTERVALS (dfo COMPARED TO bfo)			HIGHER RR INTERVALS (dfo COMPARED TO bfo)		
TIME DOMAIN	bfo	dfo	afo	bfo	dfo	afo
RR-Int	675.00	597.59*	646.15	551.63	599.69*	616.50
SDNN	52.65	37.34	48.78	42.48	41.58	52.70
RMSSD	34.36	25.56	30.37	28.75	28.56	33.29
pNN50	7.86	4.11	7.66	6.60	8.05	9.59

*The values of the RR intervals of both samples of students dfo are almost identical.

this are physical[2] and thermoregulatory activity, the renin-angiotensin system, and the influences of the endothelium on the heart.[1] As reported by Shaffer and Ginsberg,[20] experimental evidence suggests that the heart intrinsically generates the VLF rhythm and efferent SNS activity due to physical activity; a stress response modulates its amplitude and frequency. In both samples of students, VLFs values decrease dfo, although this drop is barely noticeable in I-students. They recover 99.7% of TP (compared to the 100% of the TP quantified in the other sample) afo and with slightly more difference in HFs and LFs, but less in VLFs. Therefore, we can imagine that the ANS acts on the HRV continuously with a wide-range dynamic balance. The hearts of D-students are less able to be modulated in dfo. The balance is dynamic because it would not be a simple scale, but instead a variable one in which the equilibrium point has moment arms of different lengths, together with the application of different weights (see Fig. 1E indices). This happens in other biological fields, for example: genesis of the membrane potential of cells as the result of the unequal ion distribution between the inner and outer layers of their membranes.

In conclusion, as mentioned above,[16] the amount of HRV is an energy store for better cardiac performance in eustress activities. Flight training engages regular and advanced tasks and/or emergency situations. When this happens, the total power of the heart decreases because the RR intervals are forced toward low values; this would cause a decrease in the capability of being modulated by the numerous controlling mechanisms. Flight activity involves continuous demanding tasks that can be potentially read by analysis of the HRV; a high HRV ensures better management of tasks that require a greater commitment of the cardiovascular function. Furthermore, this experimental protocol can also be useful to flight instructors for the purpose of revision during the training protocols of our students.

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Selective Serotonin Reuptake Inhibitors and Other Treatment Modalities for Deep Space Missions

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INTRODUCTION: As humankind ventures further into the depths of space, planning is already underway for long-duration exploration missions that will test the bounds of human performance. Deep space travel will include added risk related to stressors from the isolated, confined, and extreme environment that lies outside the boundaries of low Earth orbit. Currently, selective serotonin reuptake inhibitors (SSRIs) are considered the standard of care for many mental health diagnoses, including anxiety and depression; however, SSRIs are also associated with several undesired side effects. The utility of nonpharmacological therapies for the management of behavioral health conditions has not yet been fully explored.

METHODS: A comprehensive literature search was performed using PubMed. Relevant articles pertaining to the psychological impacts of isolated, confined, and extreme environments, use of SSRIs in spaceflight, side effects associated with SSRIs, and nonpharmacological treatments for anxiety and depression were reviewed. Over 70 studies were reviewed in total.

RESULTS: Reduced bone mineral density, impaired hemostatic function, significant individual variability resulting from gene polymorphisms, and drug-drug interactions are well described adverse effects of SSRIs that may complicate their operational use in the deep space environment. Four alternative therapies for the treatment of anxiety and depression may show promise for long duration missions.

DISCUSSION: Although SSRIs have long been considered standard of care treatment for many behavioral health conditions, we cannot trivialize the risk that prolonged pharmacological therapy may pose. The need to mitigate these risks by exploring alternative therapies has never been more relevant.

KEYWORDS: selective serotonin reuptake inhibitors, spaceflight, behavioral health, stressors.

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As humankind continues to venture further into the depths of space, planning is already underway for long-duration exploration missions lasting several years that will test the bounds of human performance. With this in mind, the aerospace medicine community has been hard at work developing preventative strategies and risk mitigation plans to optimize this performance and to anticipate the hazards that will affect human health and performance. One important hazard that will invariably affect the deep space traveler are the added stressors that will result from the isolated, confined, and extreme (ICE) environment that lies outside of the comfort of low Earth orbit. In addition to this stress and isolation, the space traveler must inherently be more autonomous with significantly less ground-level support for assistance given the anticipated delays that will likely hinder communication with mission control.[3] As we anticipate the human factors and psychological stressors that threaten the safety of our astronauts and their incumbent risks to mission accomplishment, mental health prevention and mitigation strategies have become exceedingly important and are a necessity for any long-duration exploration mission.[17]

Arguably, one of the most important medical breakthroughs of the 20th century in the field of psychiatry and mental health was the discovery of the class of medications known as selective serotonin reuptake inhibitors (SSRIs).[54] Currently, SSRIs are considered the gold standard treatment for many mental health

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diagnoses, including anxiety and depression.[27] Despite their known therapeutic benefits, however, SSRIs are also associated with undesired side effects. This paper will explore the history of SSRIs, their positive and negative effects, and several other novel and underexplored pharmaceutical and nonpharmaceutical therapeutic strategies that might be considered to prepare, prevent, and mitigate mental health stressors from long-duration space travel. While not synonymous, in this paper, the terms adverse effects and side effects are used interchangeably. We chose not to include psychotherapies due to the pragmatic constraints of delivering them when the communications gap is measured in minutes. Additionally, this paper will review the evidence gleaned from the literature studying mental health in ICEs. These environments serve as an analog for deep space missions as astronauts will need to be more autonomous and adaptable to changing conditions. Indeed, many of the factors indicating which individuals will successfully maintain high performance levels in isolated and confined environments remain under exploration. To date, NASA has relied heavily on astronaut selection as one of its strongest behavioral health countermeasures. Long-duration missions pose several unique challenges that will require careful selection and consideration of which candidates might be most suitable for settings involving communication delays and extreme isolation. Individuals who might be genetically predisposed and vulnerable to developing a mental health problem are of particular concern. The likelihood of the emergence of a psychiatric illness on a long-duration mission becomes greater with increased time and distance from Earth. Careful consideration, forethought, and discussion of appropriate pharmaceutical agents to treat mental illness occurring in deep space, such as SSRIs and nonpharmacological agents, need to be debated and discussed early on in mission development and planning.

The neurophysiological pathways and biochemical basis of disease in behavioral health remain a subject of intense debate and scrutiny in psychiatry and research to better understand these pathways is ongoing. The link of 5-hydroxytryptamine (5-HT, serotonin) to depression and mental health became better understood in the 1960s following the quantification of 5-HT levels in patients postmortem. Investigators found that 5-HT levels were 19% lower in the hindbrains of patients who had diagnoses of depression or “probably depressed” when compared to control subjects.[48] In the years surrounding this study, researchers set out to create a drug that solely inhibited the reuptake of serotonin. In 1971, this objective was completed by Drs. Hans Corrodi and Arvid Carlsson with the introduction of zimelidine. Shortly thereafter, fluoxetine was developed and was released for clinical use in 1988.[54] Since then, several other SSRIs have been introduced and their use has been a breakthrough for the field of psychiatry.

Mechanistically, selective serotonin reuptake inhibitors have 20–1500 times more affinity for the serotonin receptor over the norepinephrine receptor.[24] The drugs bind minimally to postsynaptic receptors (e.g., adrenergic, dopaminergic receptors), including the postsynaptic serotonin receptor. However, SSRIs do not induce the serotonin release and induce increased activity at the postsynaptic receptor almost exclusively via inhibiting the reuptake of serotonin in the synaptic cleft.[24] As a class of medications, SSRIs have numerous side effects, most of which are seen with long-term therapy. Side effects include hypotension, nausea, bone loss, bleeding dysfunction, QT prolongation, and sexual dysfunction, among others.

The Food and Drug Administration (FDA) has approved the use of SSRIs in the treatment of major depressive disorder, generalized anxiety disorder, bulimia nervosa, bipolar depression, obsessive-compulsive disorder, panic disorder, premenstrual dysphoric disorder, treatment-resistant depression, posttraumatic stress disorder, and social anxiety disorder.[12] In addition, there are additional off-label uses for SSRIs that are outside the scope of this paper. Although SSRIs do possess adverse effects as noted, many are not as salient to the spaceflight environment with respect to exploration class mission planning and are, therefore, not covered in detail within this paper. However, in order to understand the potential usage of SSRIs in the spaceflight environment, we must first review the history of psychiatric disease in aviation and spaceflight analog environments and SSRIs’ current use in these environments.

Current Use of SSRIs in Aviation and Spaceflight

Although many psychiatric diseases were previously disqualifying for flight, the aviation medicine community has eased several restrictions to allow those with prior mental health diagnoses an opportunity to participate in aviation activities. Currently an individual may be considered for a Federal Aviation Administration (FAA) Authorization of a Special Issuance of a Medical Certificate if the applicant has one of the following diagnoses: major depressive disorder (mild or moderate, either single or recurrent episode), dysthymic disorder, adjustment disorder with depressed mood, or any nondepression-related condition for which an SSRI is used. The Federal Aviation Administration (FAA)-approved SSRIs are fluoxetine, escitalopram, sertraline, and citalopram. In order to qualify with the FAA, the applicant must be clinically stable for at least 6 mo with no side effects that would affect aviation operations.

Although never used, SSRIs are part of the onboard U.S. formulary that is currently deployed to the International Space Station (ISS) for contingency use. The current psychotropic medications on the ISS are sertraline and venlafaxine (antidepressant medications), diazepam and lorazepam (anxiolytic medications), and aripiprazole and ziprasidone (antipsychotic medications). Currently, the astronauts assigned to the ISS participate in private medical conferences with flight surgeons and private psychological conferences with psychology/psychiatry behavioral health providers biweekly to address any medical or behavioral health concerns during their missions. For long-duration missions, private psychological conferences will continue to be used; however, due to communication delays, other platforms such as virtual reality and a behavioral health dashboard are currently being investigated.

With regards to commercial space programs, it remains uncertain what protocols will be used for medical and psychiatric screening and evaluation while on orbit. Although it is likely that there may be a certain degree of continuity with current medical operations, added flexibility regarding medical diagnoses and medication use is anticipated given the fact that most spaceflight participants are likely to be paying participants.

Mental Health Symptoms in Austere and Remote Environments

In order to fully appreciate the importance of preventative health and contingency planning for psychiatric disease, it is worthwhile to review the published data with regards to the development of psychiatric disease in austere and remote environments, as they are often considered the best terrestrial analogs for deep space exploration. One important trait that is felt to be advantageous for deep space missions is adaptability. Many studies aimed at better understanding the effects of ICE environments on mental health have been conducted in Earth-based space exploration analogs with varying crew numbers and time lengths. Several of these studies have concluded that emotional stability (or instability) was an important factor affecting adaptability in extreme environments.[14,15,25]

An important operational environment analog that has been well-studied in the literature is the Arctic/Antarctic. One study by Palinkas et al. conducted in personnel overwintered in Antarctica noted significant seasonal variation in depressive symptoms felt to be likely linked with social isolation and the absence of sunlight.[37] The investigators also found that marital status and summer depression were significant independent predictors of winter depression. Another study conducted by Wright et al. found that Arctic workers with low supervisor ratings were higher in psychopathology indicators and were concluded to have poor adaptability to their environment.[57] Additionally, Palinkas et al. determined the incidence of mood disorders, adjustments disorders, and sleep disorders to be as high as 4.2%, 3.8%, and 2.9%, respectively, at the end of austral winter in those working at McMurdo and the South Pole between 1994 and 1997.[38] In a specific review looking at submariners, it was found that those with depression, anxiety, and interpersonal problems had higher rates of disqualifications from duty. Failure to adapt was listed as a conclusion from these findings.[55] These studies corroborate the importance of routine screening for pre-existing mental health disorders and emphasize the importance of adaptability in subjects being deployed to ICE environments.

When examining previous and current analog missions, there has been some qualitative data to suggest the presence of negative emotions in subjects after an analog exposure. A review by Alfano et al.[1] found that overall self-reported negative emotions have been found to be low in spaceflight, long-duration space simulation analogs, and polar environments. Their group found that broad-based assessments may not detect symptoms of anxiety and depression and choosing more novel measures of emotion may be better suited.[1] These negative emotions can potentially have significant operational impacts on human performance. Additional analog studies that have demonstrated a correlation between mental health indicators and the remote environment include the Mars500 study, winter-over studies in Antarctica, the Hawai'i Space Exploration Analog and Simulation Mars analog facility, and the Human Exploration and Research Analog at NASA's Johnson Space Center.[10,33,50] Several studies conducted within these analog environments have shown that exposed subjects may be at increased risk for development of depression, stress, and anxiety.[2,6] Invariably, our prior experience in analog environments suggests that any decrements in the psychological health of our crewmembers during long-duration spaceflight may pose a real threat to the success of future missions, despite the selection of crews without a history of psychological health problems.[36]

METHODS

A comprehensive literature search was performed using PubMed and relevant articles pertaining to the psychological impacts of ICE environments, use of SSRIs in spaceflight, side effects associated with SSRIs, and nonpharmacological treatments for anxiety and depression were reviewed. Specifically, articles that referenced the hematologic side effects of SSRIs, effects of SSRIs on bone mineral density (BMD), neurocognitive effects of SSRIs, and pharmacological effects of SSRIs were reviewed. Common search terms used included "bone loss in spaceflight," "hematologic effects of SSRIs," "neurocognitive effects of SSRIs," "hematologic effects of spaceflight," "effects of spaceflight on bone density," "stress and anxiety in spaceflight analog," and "non-pharmacologic treatment of anxiety and depression." Over 70 studies were reviewed in total.

RESULTS

Hematologic Effects of Spaceflight and SSRIs

Although selective-serotonin reuptake inhibitors have been considered safer than previous classes of psychotropic medications and have often boasted a more favorable side effect profile, many SSRIs have been found to alter hemostatic functions and, in particular, impair hemostasis. Numerous mechanisms have been thought to contribute to this effect, including nitric oxide inhibition, blockade of platelet calcium mobilization, and reduction of platelet factors leading to decreased expression of platelet activation.[53] Meta-analysis revealed an association between SSRI use and increased risk of severe bleeding (odds ratio: 1.41, 1.27–1.57). Severe bleeding was defined as the need for prompt intervention of a healthcare professional or reoperation after surgery. The estimated increase in risk of bleeding was on average 36% in this meta-analysis.[29] Given the possible increased risk of bleeding and altered hemostatic function related to SSRI use, the prolonged use of these medications is not inconsequential, especially with the increased operational demands of exploration class missions and the higher probabilities of traumatic or accidental injury with the longer durations of spaceflight that would invariably result. In fact, a recent meta-analysis by Anglin et al. found that when SSRIs are used in combination with nonsteroidal anti-inflammatory drugs, subjects had a significant increase in upper gastrointestinal bleeding compared to both SSRI alone and control groups.[4] This has broad operational implications for long duration exploration class missions given the relative ubiquitous use of nonsteroidal anti-inflammatory drugs for analgesia during spaceflight activities.

Bone Density Effects of Spaceflight and SSRIs

Bone demineralization and reduced bone density are well established consequences of microgravity exposure and have consistently been observed in astronauts throughout the history of human spaceflight following mission completion. Although primarily a result of the loss of mechanical loading secondary to microgravity, other important factors have been implicated, including dietary factors such as high sodium and animal protein intake, increased ambient levels of carbon dioxide, and reduced 1, 25-Vitamin D conversion related to reduced sun exposure.[16] Since 1998, NASA has medically required the use of dual X-ray absorptiometry (DXA) to screen and quantify areal bone density in astronauts given the risk of microgravity exposure to bone health and it has been extensively used to quantify bone losses from spaceflight in experimental studies.[35] Subsequent studies have also used high resolution peripheral quantitative computed tomography to study bone morphology and architecture by obtaining volumetric bone mineral density levels.[13] Due to the morbid nature of the procedure, there is a paucity of data on bone loss in spaceflight that have used bone histomorphology for evaluation.

While there are many factors that may contribute to the bone loss associated with spaceflight and their implications, one important and underrecognized adverse effect of SSRI use is the inhibitory effect on normal bone remodeling. Ortuno et al. showed that the extent of SSRI use likely mediates its effect on bone mass.[34] In this rodent study, a dual mechanism of action was demonstrated where in short term use (3 wk), treatment with fluoxetine (Flx) resulted in a local antiresorptive response which increased bone mass; however, with prolonged use of Flx (6-wk use), a net loss of bone occurs which is mediated by a centrally triggered increase in sympathetic activity. Researchers studied wild-type female mice treated with either 3 wk or 6 wk of Flx to achieve levels comparable to therapeutic plasma levels in humans and observed its effect on long bones and vertebrae. They found that the mice treated with Flx for 3 wk had lower osteoclast surface, whereas bone formation rate and osteoblast surface were not affected. In contrast, mice treated with Flx for 6 wk had no effects on osteoclast surfaces; however, the osteoblast surface and bone formation rate were significantly lower. The second effect is associated with decreased serotonin signaling in the hypothalamus and increased sympathetic nervous system activity, which is mitigated by coadministration of low dose propranolol. Calarge et al. studied the skeletal effects of SSRI use on older adolescents by performing a 2-yr prospective study that examined bone density using whole body DXA and lumbar spine DXA at study entry and every 8 mo and calculating volumetric bone mineral density at the nondominant radius using peripheral quantitative computed tomography at study entry and every 4 mo of participants ages 15–20 yr old.[9] After adjusting for potential confounders such as depression severity, the researchers found that SSRI use was associated with increasing lumbar spine areal bone mineral density and bone formation in female participants, but decreasing lumbar spine areal bone mineral density in male participants. Haney et al. examined the link between SSRI use and reduced bone mineral density (BMD) in a review published in *Bone* in 2009.[21] Several cross-sectional studies have suggested a link between lower BMD and SSRI use in both men and women. Longitudinal studies have also shown that SSRI users have a 1.6-fold greater decline in BMD compared to nonusers. An increase in fracture risk in SSRI users has also been noted in case-control studies done in large administrative datasets. However, mixed results have been noted when studying reduced BMD in association with increasing dose and duration of SSRI. Additionally, many studies have found that depression is an independent risk factor for decreased BMD, making it difficult to disentangle the causal relationship between SSRI and reduced BMD. Despite this, Haney et al. concluded that, based on the mounting evidence suggesting a causal relationship between reduced BMD and SSRI use, SSRIs should be listed among medications that contribute to the development of osteoporosis. Zhou et al. performed the first meta-analysis to study the relationship between SSRI use on BMD in 2018.[59] The researchers selected 11 studies that examined the effect of SSRI use on bone density and found that the use of SSRIs was significantly associated with lower BMD values of the lumbar spine, but not of the total hip or femoral neck. Additionally, SSRI use was associated with greater BMD loss in older people. Rawson et al. studied the effects of venlafaxine treatment in older adults with depression and found that levels of bone turnover products change in a pattern that suggests accelerated bone loss.[44] Although venlafaxine is a serotonin-norepinephrine reuptake inhibitor and not an SSRI, these findings suggest that further examination of its use in deep space missions is warranted given its inclusion in the ISS formulary.

With our visions set toward the lunar and Martian surfaces, the importance of strategies to mitigate and counter bone losses in spaceflight participants has become exceedingly important. While data regarding fracture risk in the microgravity environment have not been clearly elucidated given our limited operational experience, low incidence, and lack of generalizability of validated fracture risk assessment tools, there remains concern that clinically meaningful bone loss may occur in any exploration-class mission.[30] The long-term use of SSRIs potentially adds to and confounds this risk by introducing a pharmacological means of accelerating bone loss and should prompt further study into alternative methods for the treatment of anxiety, depression, and other mental health disorders where SSRIs may be historically indicated.

Neurocognitive Concerns for Long-Duration Spaceflight and SSRIs

The risks from SSRIs in long-duration spaceflight are not clear. A concern is whether use of SSRIs, separate from the underlying disease, will lead to neurocognitive impairment. Information available is limited. Most studies of SSRIs are in individuals with illness. We are unaware of studies of long-term use in healthy controls. In a study of 50 depressed patients followed for 8 wk, there was a significant ($P < 0.0001$) decline in Mini-Mental State Examination scores consistent with a decline in function during the first 2 mo of treatment.[47] In a 6-mo study of patients with depression or anxiety, 20% of the patients reported cognitive symptoms including fatigue, inattentiveness, decreased concentration, apathy, and memory difficulties.[40] In contrast to the above two studies, in a meta-analysis of 33 studies, no significant neurocognitive effects were observed in healthy individuals.[42] In patients with depression, modest positive effects were observed, including executive function, divided attention, processing speed, recent memory, sustained attention, and divided attention.

Aeromedical regulators are concerned about aviators with untreated psychiatric disorders as well as the effects of an SSRI. In 2004, an Aerospace Medical Association report urged certification authorities to develop protocols to manage adverse effects from SSRIs and to consider their safe use in aviators without negative side effects.[26] Historically, the Federal Aviation Administration required neuropsychological testing of individuals taking SSRIs prior to granting a special issuance, out of concern the medications themselves may impact the aviator's performance. For many years, they also required routine retesting of aviators still taking SSRIs. With over a decade of experience, they found repeat neuropsychological testing did not yield useful information in the majority of aviators, so within the past year they ceased requiring routine neuropsychological retesting. They only require cognitive retesting if there are unique individual circumstances. As of the time of this paper, the Federal Aviation Administration, the United States' certification authority, allows the use of four specific SSRIs, monitoring aviators using cognitive testing, with an instrument specifically designed to assess aviator neurocognitive functions.[51]

There are obvious consequences of crewmembers experiencing common psychiatric illnesses with known neurocognitive effects during a long-term spaceflight. Some available research raises the possibility of negative neurocognitive consequences from SSRIs while others do not. Operational medical decision making will need to balance crew selection while considering the known deleterious effects of illnesses such as depression and anxiety, and the possible effects of long-term SSRI usage.

Pharmacological Concerns for Spaceflight and SSRIs

Seven SSRIs are currently marketed in the United States: fluoxetine, fluvoxamine, paroxetine, sertraline, vilazodone, escitalopram, and citalopram. The last two, escitalopram and citalopram, are therapeutically the same drug because escitalopram is the (S)-enantiomer of racemic citalopram, and the therapeutic effects of citalopram are mediated by the escitalopram. Although all SSRIs have broadly similar antidepressant effects pharmacologically, they have important pharmacokinetic distinctions.

All SSRIs undergo significant hepatic metabolism as a step in their elimination from the body. Consequently, factors that affect their metabolism can have significant effects on drug exposure. The two greatest pharmacokinetic concerns are drug-drug interactions and gene polymorphisms of the liver cytochrome P450 (CYP) xenobiotic-metabolizing enzymes. CYP enzymes are responsible for metabolism of a large proportion of drug substances. Two isoenzymes in particular, CYP2D6 and CYP3A4, are responsible for metabolism of more than half of all orally effective drugs, including SSRIs.[39] In addition, some SSRIs undergo significant metabolism by isoenzymes CYP2C9 and CYP2C19 (**Table I**).

A common cause of drug-drug interactions is when one drug interferes with the metabolism of another. In the case of SSRIs, drugs that interfere with CYP2D6 can inhibit the metabolism of paroxetine, fluoxetine, and fluvoxamine. Similarly, interference with CYP2C19 can significantly increase exposure to citalopram, escitalopram, and sertraline. SSRIs may also affect the metabolism of other drugs. As shown in Table I, fluoxetine and paroxetine are inhibitors of CYP2D6, which can affect a broad array of drugs. Fluvoxamine, together with its metabolites, inhibits several important CYPs, making it especially prone to increasing exposure to other liver-metabolized drugs. Notably, citalopram, escitalopram, and sertraline are thought to have minimal effects on cytochrome P450 enzymes, which gives these SSRIs an advantage in the context of clinical polypharmacy. Gene polymorphisms are common contributors to variability in individual response to drug treatment and susceptibility to adverse effects. Many CYP genes are highly

Table I. Summary of Key Pharmacokinetic Characteristics of SSRIs.[23,43,49]

SSRI	$t_{1/2}$	APPARENT Vd ($L \cdot kg^{-1}$)	LINEAR KINETICS	METABOLIZING ENZYMES	INHIBITED CYP
Citalopram	36 h	14–16	Yes	**CYP2C19**, CYP3A4, CYP2D6	Minimal
Escitalopram	27–33 h	15	–	**CYP2C19, CYP2D6,** CYP3A4	Minimal
Fluoxetine	1 to 4 d	20–45	No	**CYP2D6, CYP2C9**, CYP2C19 CYPCYP3A	2D6
Fluvoxamine	15 h	5	No	**CYP2D6**, CYP1A2	1A2, 2D6, (2C19)
Paroxetine	20 h	3–12	No	CYP2D6, catechol-O-methyltransferase,	**2D6**
Sertraline	26 h	20	Yes	**CYP2C19,** CYP2D6, CYP3A4	Minimal

SSRI: selective serotonin reuptake inhibitor; t1/2: half-life; Vd: apparent volume of distribution; CYP: cytochrome P450 enzymes.
Bolded CYPs indicate primary metabolism pathway; CYP enzymes in parentheses indicate indirect effects of metabolites.

polymorphic[18] and allele frequency can vary substantially among racial and ethnic groups.[41] For this reason, gene polymorphisms are an important clinical consideration as NASA strives to increase ethnic and racial diversity of the astronaut corps and the role of polymorphism should be seriously considered when selecting SSRIs for Earth-independent medical care. For example, CYP2D6 has a very large number of haplotypes that produce highly variable functional activity classified into four levels of activity ranging from poor to ultra-rapid metabolizers. The complete loss of CYP2D6 enzyme activity is rare in Asian populations, with a frequency of around 10% of the Caucasian, Hispanic, and African populations.[8,43] Conversely, ultra-rapid metabolizer phenotypes are reported to be less than 5% of Caucasians and African Americans, but up to 30% of Ethiopians and Saudi Arabians.[43]

Multiple studies have demonstrated that CYP2D6 ultrarapid metabolizers have low or undetectable paroxetine plasma concentrations, contributing to therapeutic failure of paroxetine and potentially fluvoxamine. For such individuals, it is reasonable to select an alternative SSRI that is not extensively metabolized by CYP2D6. Conversely, poor metabolizers have significantly greater exposures to paroxetine and fluvoxamine.[11,22] Consequently, the product label contains caution for the use of these SSRIs in patients with reduced CYP2D6 activity.

CYP2C19, like CYP2D6, is also highly polymorphic, with a distribution of functional activity that varies according to ethnicity. For example, a nonfunctional allele is present in approximately 15% of Caucasians and Africans, and up to 30% of Asians. An ultra-rapid allele has a reported frequency of 16 to 21% among Caucasians and Africans but is rare among Asians. CYP2C19 ultrarapid metabolizers have significantly lower exposure to citalopram, escitalopram, and sertraline, and increased concentrations of these drugs have been observed in poor metabolizers, which may increase the risk of adverse drug reactions. Label dosing instructions for citalopram and sertraline (but not escitalopram) recommends reducing the starting dose by 50% in poor metabolizers or using an alternative SSRI not metabolized by CYP2C19 due to the risk of QT prolongation.[22] Other CYP enzymes involved in SSRI metabolism may be rarely impacted by genetic polymorphisms (CYP3A4), or may have significant alterations in activity but play only a minor role in SSRI metabolism (i.e., CYP1A2, CYP2C9).

It is important for clinicians to be aware of the potential for drug-drug interactions and gene polymorphisms, particularly those that reduce SSRI metabolism. This knowledge enables clinicians to anticipate the need for adjusting a patient's dose or avoid particular products altogether. Since the U.S. FDA has already warned of the risks of QT changes and serotonin syndrome in individuals with reduced metabolism and package inserts contain warnings, particularly for poor metabolizers, the potential of drug-drug interactions and genetic polymorphisms should be anticipated prior to exploration missions.

Alternative Therapies to Consider

Many studies have been conducted to examine the efficacy of non-SSRI, alternative therapies for depression and anxiety. Transcranial magnetic stimulation (TMS) has been examined over the past several decades as a potential nonpharmacological therapy for depression. This therapy involves application of a strong, pulsed magnetic field to a region of the brain to induce local neuronal depolarization and generation of action potentials. Garnaat et al. noted that multiple meta-analyses found therapeutic benefit of low-frequency, high-frequency, and bilateral TMS for depression compared to sham.[20] Furthermore, three large multisite, sham-controlled randomized controlled trials confirmed these findings and found that TMS was effective as monotherapy for depression in treatment-resistant patients, setting the basis for FDA approval of the first TMS device for depression in 2008.[20] Given that many TMS protocols require sessions >30 min long, Bakker et al. conducted a study to examine the efficacy of shortened theta burst stimulation (iTBS) protocols and found comparable results to the longer TMS protocols.[5] Blumberger et al. conducted a randomized, multicenter noninferiority study to compare the efficacy, safety, and tolerability of iTBS compared to standard 10-Hz rTMS and found iTBS to be noninferior in patients with treatment-resistant depression.[7]

Cranial electrotherapy stimulation (CES), or Alpha-Stim, is another alternative therapy for depression and anxiety that has been well studied over the years and uses small microcurrents which stimulate neurotransmitter activity in the brain to induce relaxation.[7] Morriss et al. studied the cost effectiveness and efficacy of Alpha-Stim cranial electrotherapy stimulation in patients with moderate to severe generalized anxiety disorder and found that, in patients who did not respond to low intensity psychological treatment, Alpha-Stim CES may be effective after treatment and up to 3 mo later and is cost effective.[32] Kirsch and Nichols published a review on the use of CES and concluded that it is an effective therapy with a side effect profile that is mild and self-limited that can be used as a first-line or adjuvant treatment for anxiety, depression, and insomnia and may have a role given its cost effectiveness and noninvasiveness compared to other neurostimulation techniques.[28]

Transcranial ultrasound has also been examined as a noninvasive neuromodulation method that has many advantages over TMS such as being able to noninvasively target areas of the brain with precision, but a distinct advantage over TMS in that it can also target deeper areas of the brain. Animal studies by Zhang et al. have shown that low-intensity pulsed ultrasound can ameliorate depression-like behavior in rats and transcranial ultrasound has been hypothesized by Tsai to be an alternative treatment of major depressive disorder as a single or supplemental antidepressant therapy.[52,58] Indeed, Reznik et al. explored this hypothesis by conducting a double-blind pilot study of transcranial ultrasound as a 5-d intervention and found that active delivery of transcranial ultrasound decreases worry after five sessions in patients with depression compared to placebo.[45]

Other pharmacological therapies have also been examined for the management of anxiety and depression. One such treatment that has garnered increased attention in the psychiatric community is ketamine. Although intravenous ketamine has a relatively well-established antidepressant effect, oral, intramuscular, and sublingual formulations have been recently studied given its ease of administration. Rosenblat et al. conducted a systematic review of the use of oral ketamine as a treatment for depression and found that, although the onset of action was not as rapid as with intravenous ketamine, oral ketamine was effective as an antidepressant, with good overall tolerability.[46] Sublingual ketamine has also been used with good results for patients who have required intravenous ketamine for the management of depression. McGirr et al. conducted a meta-analysis and systematic review of the literature to determine the efficacy of ketamine in major depressive episodes and found that single administrations of ketamine were efficacious in the rapid treatment of unipolar and bipolar depression.[31] In fact, a systematic review and meta-analysis conducted by Witt et al. also found that single-dose ketamine was beneficial in acute suicidality as it has been shown to have short-term benefits on suicidal thoughts for up to 72 h.[56] However, significant concern continues to exist regarding the tolerability of ketamine for routine use as a treatment for depression. Indeed, Galvez et al. performed a randomized, double-blind, placebo-controlled pilot study to examine the efficacy and tolerability of intranasal ketamine for treatment-resistant depression, but found that intranasal ketamine was not a useful treatment for depression given its variable absorption and poor tolerability in the study participants.[19] Nonetheless, ketamine is currently being deployed to the ISS for its anesthetic effects; therefore, exploration of off-label use may be warranted. Further study of these alternative therapies is indicated to explore their utility in spaceflight and other remote environments given the potential side effects of SSRIs previously noted.

DISCUSSION

With the renewed interest in deep space travel, planning of exploration class missions, and the likelihood of increased prevalence of psychiatric illness and mental health disorders in spaceflight participants, we must be ready to address and mitigate the risk of acute mental health issues arising in our spacefaring population. Although SSRIs have long been considered standard of care treatment for depression and anxiety, we cannot trivialize the risk that pharmacological therapy with SSRIs may pose to spaceflight participants given the well-documented adverse effects that may be encountered in long-term use. As humankind ventures beyond low Earth orbit and toward long-duration exploration class missions, the prolonged exposure to the microgravity environment has highlighted the necessity to mitigate the risk to bone health and reduced bone density. Although never tested experimentally, there is reason to hypothesize that the combination of SSRI use and prolonged microgravity exposure may potentially contribute to additive effects on bone mineral density and hasten the deleterious effects of each factor on bone health. While countermeasures such as resistive exercise have been the mainstay of prevention, the ability to mitigate the combined risk of these additive, negative effects on bone health may be limited during deep space exploration missions given mission requirements and volume restrictions of potential space vehicles limiting accommodations of countermeasures hardware. Additionally, prolonged exposure to SSRIs may inhibit normal hemostatic function and pose operational risks to the astronaut and mission given a potential increased likelihood of bleeding complications related to trauma and injury during exploration class missions.

From a human health and performance perspective, the need to address our treatment algorithms for anxiety and depression as we travel into deep space cannot be understated. As we begin to integrate the medical and psychological needs of an increasingly commercialized spaceflight enterprise, the need to test and develop alternative pharmacological and nonpharmacological therapies on anxiety and depression will be necessary to treat these conditions without exposing our spaceflight participants to the potential adverse effects of SSRI therapy.

The space medicine community must anticipate the challenges of the human system as we venture into deep space and develop risk mitigation strategies to the various health effects that the spaceflight participant will face. Although currently the standard of care for the treatment of anxiety and depression, SSRIs possess various side effects that the astute space medicine provider must consider when developing treatment plans for use in the microgravity environment, especially with prolonged use. Although the benefits of treatment with short-term and terrestrial use may outweigh the risks, our risk matrices may necessitate adjustment when exploring more prolonged use in the microgravity environment. With the rapid growth of the commercial spaceflight industry and imminent return to the Moon, we cannot be complacent with ensuring the human system is prepared for the physiological and psychological challenges that await. The time to explore other alternative pharmacological and nonpharmacological therapies is now.

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Wire Strikes and In-Air Obstacle Collisions During Agricultural Aviation Operations

Hannah M. Baumgartner

INTRODUCTION: Wire strikes and in-air collisions with obstacles are a leading cause of accidents in the aerial application industry. While some of these collisions occur due to unseen obstacles, some pilots report being previously aware of the obstacles that they collide with. Whether or not pilots are aware of obstacles pre-collision is an important factor to inform methods of accident prevention.

METHODS: Final reports from the National Transportation Safety Board were analyzed for Part 137 Agricultural Operation accidents that took place between January 2020 and December 2022. A deeper analysis of cases that involved an in-air collision with an obstacle was performed, excluding cases that were attributable to an external cause (e.g., aerodynamic stall). The pilot's awareness of the obstacle pre-accident was inferred from accident narratives if available.

RESULTS: Nearly half of all accidents ($N = 45$ of 107) involved an in-air collision with an obstacle (e.g., wire, tree, pole) as the defining event. In cases where pilot awareness of the obstacle was determinable through the accident report, over half of pilots ($N = 21$ of 39) had previously seen this obstacle yet still made contact with it.

DISCUSSION: In-air obstacle collisions make up a substantial portion of accidents within Part 137 Agricultural Operations. Nearly half of pilots were already aware of the obstacle before collision, indicating that inadequate preparation in scoping the field is not a predominant driver of these events. Instead, these findings suggest that other factors including distractions, high task difficulty, and errors in decision-making may contribute.

KEYWORDS: general aviation, accident analysis, human factors.

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Aerial application or agricultural aircraft operations involve the use of an aircraft to dispense fertilizer, seeds, and crop protection products to directly affect agricultural outcomes.[3] These operations are associated with a number of unique hazards and challenges, including scheduling issues due to seasonal crops, obstacles associated with flight at very low altitude, and high attentional demand for single pilots and dispensing equipment operation. These risks are reflected in accident data, and between 2017 and 2021, there were 290 accidents in Part 137 Agricultural Operations, with 44 of those accidents being fatal.[4] Further, a 2014 National Transportation Safety Board (NTSB) Special Investigations Report on agricultural operations identified safety issues related to lack of operations-specific guidance for fatigue, risk management, and pilot knowledge and skills tests among their list of safety issues in this industry.[5]

Despite many of these safety issues or unique hazards being related to human factors, there is limited research on human factors within agricultural operations. One previous analysis showed that 41 of 44 accidents in Australian agricultural operations from 2000–2005 were related to human performance failures using the Human Factors Analysis and Classification System approach.[2] The most frequently reported occurrence in this analysis was wire strikes, which were involved in 13 of 44 human-factors-related accidents.

Wire strikes and in-air collisions with obstacles are a leading cause of accidents in agricultural operations. Indeed, the

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2014 NTSB Special Investigations Report identified in-flight collision with an obstacle among its top three consistent defining events in historical accident data.[5] Today, in-flight collisions with obstacles continue to be one of the most prevalent defining events in agricultural accidents. Understanding how these accidents occur is critical to preventing future similar accidents. However, no data currently exist to quantify the prevalence of wire strike and in-air obstacle collision accidents, nor the prevalence of pilot awareness of obstacles pre-collision.

It may be presumed that these accidents largely occur due to collision with previously unseen obstacles. However, some pilots report being previously aware of the obstacles that they collide with and have already completed multiple passes on a given field at the time of the accident. Whether or not pilots are aware of obstacles pre-collision in these agricultural aviation accidents is an important factor to inform methods of accident prevention.

The current report describes an analysis of wire strike and in-air obstacle collision accidents in agricultural operations, with a specific focus on whether pilots were previously aware of the obstacle before collision. Results from this research can inform targeted approaches to reduce future wire strike accidents in agricultural operations by informing best practices for avoidance.

METHODS

Final accident reports from the NTSB were retrieved for all Part 137 Agricultural Operation accidents in the United States that took place between January 2020 and December 2022. Final reports and associated dockets from completed investigations were reviewed. Narratives, demographic data, probable cause, and findings were evaluated for overall trends across accidents. A deeper analysis of cases that involved an in-air collision with an obstacle was performed, excluding cases that were attributable to an external cause (e.g., aerodynamic stall, mechanical or computer failure). For cases that involved an in-air collision with an obstacle as the primary cause of the accident, the pilot's awareness of the obstacle pre-accident was inferred from accident narratives if available.

For the purposes of this analysis, pilots were deemed to have been previously aware of the obstacle if: 1) awareness was explicitly reported in the final report; or 2) awareness was inferred from the final report due to description of having maneuvered around the obstacle in previous passes. A lack of previous awareness of the obstacle by the pilot was determined if this was explicitly stated in the accident report. Cases where previous awareness of the obstacle was undeterminable, such as in the case of most fatal accidents, were coded as "unclear" in the current analysis.

RESULTS

A total of 107 final accident reports from Part 137 Agricultural Operations between Jan. 1, 2020, and Dec. 31, 2022, were identified. Of these accidents, 13 included fatal injuries, 11 included serious injuries, and 19 included minor injuries.

In-Air Obstacle Collisions

Nearly half of all accidents (N = 48) included in-air collisions with an obstacle such as a wire, tree, or pole. Of these accidents, only three in-air obstacle collisions were secondary to another immediate accident cause such as an aerodynamic stall or computer/mechanical failure. Therefore, the remaining 45 in-air obstacle collisions were further analyzed for accident trends and pilot awareness of the obstacle (**Table I**).

Of the 45 in-air obstacle collisions, strikes most often occurred with telephone or power lines (N = 32). Less frequent obstacles included trees (N = 6), poles (N = 2), crops (N = 2), windmills (N = 2), and towers (N = 1). These accidents included seven with fatal injuries, eight with serious injuries, and eight with minor injuries. Pilots (N = 45 men) were on average 47 yr old (SD: ± 15 yr) with an average of 9156 h (SD: ± 9505 h) of flight time experience (**Fig. 1**).

Previous Awareness of Obstacle

In cases where pilot awareness of the obstacle was determinable through the accident report or investigation docket, over half of pilots (N = 21 of 39 accidents) had previously seen this obstacle yet still made contact with it (**Fig. 2**). For some accidents, confirmation of awareness was obtained through explicit mention by the pilots in the final accident reports. For example, pilots noted "Even though I knew that the powerline was there, I neglected to climb high enough to clear the powerline…" (NTSB Accident No. CEN22LA200) or "I was fully aware of the position of the wind turbines and the wires in these fields as I had scouted them very well the day before" (NTSB Accident No. CEN21LA349). Confirmation of prior awareness of the obstacle was also inferred in cases where the pilot had already maneuvered around the obstacle during previous passes along the field. For example, reports were included with statements such as "During his third pass of the morning, he underestimated the top of the corn in the middle by about two feet" (NTSB Accident No. CEN22LA340) or "The accident occurred during the pilot's 21st pass over the field that day, and the pilot had been maneuvering to avoid the wire numerous times prior to the accident" (NTSB Accident No. CEN21LA225).

There were 18 accident reports that indicated that the pilot was previously unaware of the obstacle's location before the in-air collision (Fig. 2). These cases were identified due to explicit mention of this in the accident investigation reports, including comments such as "Upon approaching 1st pass I encountered previously unseen powerlines (obscured by trees and terrain)" (NTSB Accident No. WPR20CA179) and "I did not see the wire until it was too late to jump over it" (NTSB Accident No. CEN21LA148). For 6 of the 45 cases of in-air obstacle collisions, it was unclear from the final accident report or associated docket whether the pilot was previously aware of the obstacle prior to collision.

Table I. In-Air Obstacle Collision Accidents in Agricultural Operations.*

NTSB NUMBER	OBSTACLE TYPE	AWARE OF OBSTACLE?	HIGHEST INJURY LEVEL	PILOT AGE	PILOT FLIGHT TIME (est)	NOTE
CEN22LA387	Wire	Yes	None	31	1020	
CEN22LA366	Wire	Yes	None	32	1100	
CEN22LA359	Tree	No	Minor	45		
CEN22LA350	Wire	No	None	37	4104	
CEN22LA345	Wire	No	None	32	1010	
CEN22LA340	Crop	Yes	None	37	814	
CEN22LA342	Wire	Yes	None	48	2641	
CEN22LA371	Windmill	Yes	None	34	4300	
CEN22LA248	Pole	Yes	None	75	24,000	
CEN22LA226	Pole	Yes	Serious	57	16,000	Awareness inferred from previous passes in field.
CEN22LA200	Wire	Yes	Minor	48	2890	
WPR22LA140	Wire	No	Minor	62	2336	
CEN22LA006	Wire	No	Minor	25	2941	
CEN21LA421	Wire	Yes	None	25		
WPR21LA338	Wire	Yes	None	40	3349	
WPR21LA333	Tree	No	Serious	67	29,000	
CEN21FA368	Wire	Yes	Fatal	63		Awareness inferred from previous passes in field.
CEN21LA356	Wire	No	Serious	29	1600	
CEN21LA354	Wire	Yes	Serious	24	1037	
CEN21LA350	Wire	No	Minor	66	27,652	
CEN21LA349	Wire	Yes	Serious	54	7321	
CEN21LA348	Wire	Yes	Serious	31	3360	
WPR21LA310	Windmill	No	Serious	61	3041	
CEN21LA339	Wire	No	Minor	53		
CEN21LA452	Wire	No	None	47		
CEN21LA313	Crop	Yes	None	27	1865	
CEN21LA318	Tower	Unclear	None	42	11,428	
ERA21LA270	Wire	No	None	34	2554	
CEN21LA283	Tree	Unclear	Serious	66	27,100	
CEN21LA225	Wire	Yes	Fatal	47	4500	Awareness inferred from previous passes in field.
ERA21FA200	Wire	Yes	Fatal	57	6670	Awareness inferred from previous passes in field.
WPR21LA130	Wire	Unclear	Minor	36	10,000	
CEN21LA148	Wire	No	None	56	14,639	
CEN21LA113	Wire	Unclear	Fatal	68	30,000	
CEN21LA005	Tree	Unclear	None	32	1090	
ERA20LA330	Tree	Yes	Fatal	67	31,000	Awareness inferred from previous passes in field.
CEN20CA347	Wire	Yes	Minor	65	18,671	
CEN20CA311	Wire	No	Minor	28	1880	
CEN20CA312	Wire	Yes	None	48	11,997	
CEN20CA300	Wire	No	None	42	7700	
ERA20LA220	Wire	No	Fatal	65	19,340	
WPR20CA179	Wire	No	None	55	9693	
WPR20CA171	Wire	No	Minor	65	17,021	
CEN20LA143	Tree	Unclear	Fatal	46	10,000	
CEN20LA109	Wire	Yes	None	53	7867	

*These results are from the analysis of the 45 final NTSB accident reports from 2020–2022 that involved an in-air obstacle collision as the primary cause of the accident in Part 137 Agricultural Operations.

DISCUSSION

This brief report describes characteristics of a particularly frequent type of accident in the Part 137 Agricultural Aviation industry, in-air obstacle collisions. Though wire strikes and similar in-air obstacle collisions are known to be consistent defining events in historical agricultural accident data,[2] little research has examined the human factor issues associated with these accidents to understand why they occur. The current study therefore evaluated common characteristics of these accidents using final reports from NTSB investigations from Jan. 2020 to Dec. 2022, with a particular focus on whether the pilot was already aware of the obstacle pre-collision.

Overall, these findings confirm the prevalence of in-air obstacle collisions, which accounted for nearly half of all defining events in accidents from this sample. The most frequently hit obstacle in these accidents were wires, though some instances of hitting trees, poles, windmills, crops, and towers were noted. The vast majority of these collisions were also not attributable to another immediate event, such as an aerodynamic stall or computer/mechanical failure. Further, these accidents were prevalent across a range of pilot demographics, including pilots

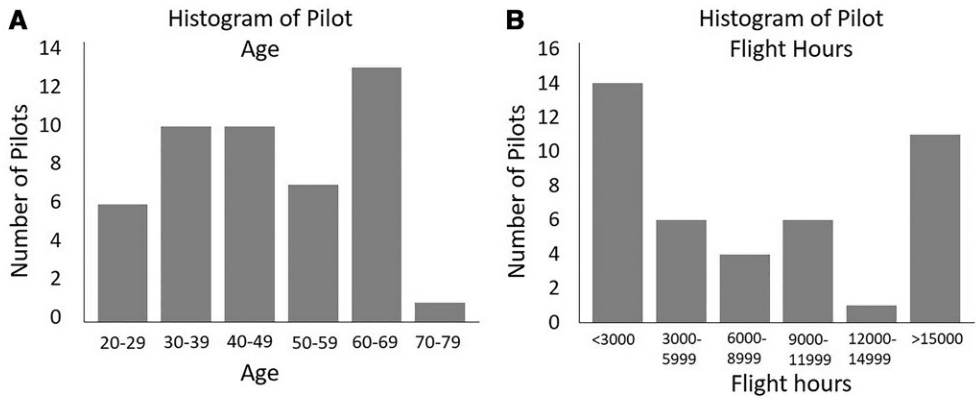

Fig. 1. Demographics of pilots who experienced in-air obstacle collisions. A) Ages of pilots included in NTSB final accident reports for the 45 evaluated in-air obstacle collisions are shown in a histogram. B) A histogram shows the range of flight hours attributed to the pilots who experienced in-air obstacle collisions.

both young and old and pilots with extensive or few total flight hours. However, the histogram of pilot flight hour time (Fig. 1B) demonstrates a U-shaped distribution of flight experience in pilots involved in these collisions. Given the prevalence of pilots that had either <3000 h flight time or >15,000 h flight time, this suggests that contributing factors may include pilot inexperience and pilot complacency, respectively. However, it should be noted that without wider demographic information about agricultural pilots, it is unclear whether this U-shaped distribution simply corresponds to the overall flight hour distribution in the agricultural pilot population.

Of note, about half of all pilots involved in these in-air obstacle collisions were previously aware of the obstacle before collision. Typically, this was evident from the investigation report that noted that the pilot was aware of the obstacle through prior scouting, discussions with the property owner, or having previously flown passes on the field around the obstacle. These findings imply that other factors, including distractions, high task difficulty, and errors in decision-making, may contribute to these frequent accident types. Mitigations that solely focus on awareness and preflight preparations around the field will not be sufficient in combatting these accidents. Instead, a human-factors-informed approach, such as additional training or targeted advertisements on pilot complacency,[1,6] may be key in promoting awareness of the causes behind these collisions and preventing future accidents.

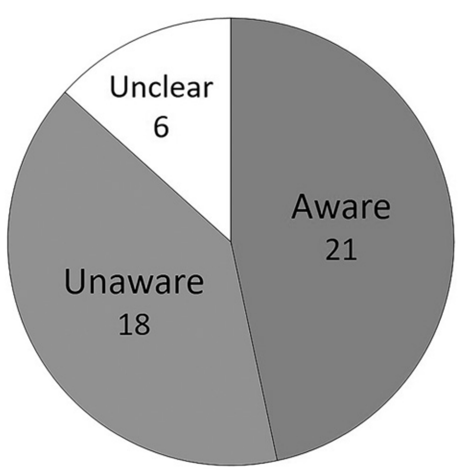

Fig. 2. Previous awareness of obstacle before in-air obstacle collision. Pilot awareness of obstacles before in-air collision was assessed through final accident reports. Pilots were categorized as either being previously aware of the obstacle ($N = 21$), unaware of the obstacle ($N = 18$), or awareness was undeterminable through the accident report ($N = 6$).

One major limitation of the current analysis is that the true prevalence of wire strikes and in-air accident collisions may be hard to determine. Events may go unreported if damage to the aircraft or other property is minimal. Therefore, the true scope of this issue and associated characteristics may not be fully represented within NTSB final accident reports, and more research is necessary to fully evaluate this accident type.

Overall, these preliminary findings indicate that future research into the causes of wire-strike events and in-air obstacle collisions within agricultural operations is necessary given the prevalence of these accidents and lack of current research.

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A 3D-Printed Portable Sterilizer to Be Used During Surgical Procedures in Spaceflight

Erika Kovalski; Linda Salazar; Dana Levin; Tovy Haber Kamine

INTRODUCTION: During spaceflight, it is important to consider the mechanisms by which surgeries and medical procedures can be safely and efficiently conducted. Instruments used to carry out these processes need to be sterilized. Thus, we have designed and tested a three-dimensional-printed (3D-printed) portable sterilizer that implements far ultraviolet-C (Far UV-C) light radiation to disinfect bacteria and microorganisms from surgical instruments.

METHODS: The sterilizer was 3D-printed with polylactic acid filament. Effectiveness was assessed through three trials at differing times of sterilization and compared against a control group of no sterilization and against Clorox wipes. Cultures were incubated on agar dishes and counted with ImageJ.

RESULTS: Increasing time under Far UV-C light radiation increased the percentage of sterilization up to 100% at 10 min. The 3D-printed sterilizer was significantly better than Clorox wipes and control.

DISCUSSION: As sterilization will be necessary for surgical procedures in microgravity and upmass is a significant concern, we have successfully demonstrated a 3D-printable portable sterilizer for surgical instruments that achieves 100% success in using Far UV-C light to disinfect its surface of bacteria with a 10-min sterilizing time. Further research is necessary to test this design in microgravity and with differently sized and shaped instruments.

KEYWORDS: 3D-printing, sterilizer, medical, space.

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With increased numbers of people traveling further from Earth, the risk of medical events requiring procedures increases. During long-duration spaceflight, humans may experience trauma, infections, and medical emergencies, which can threaten the lives of crewmembers and result in loss of mission.[4] As a result of this, it is critical to consider the mechanisms by which individuals in space can undergo medical or surgical procedures as needed. Not only must qualified medical personnel be available to perform procedures,[8] but appropriate equipment and instruments must also be available. Thus, a medical infrastructure should be thoroughly developed to promote successful medical care during spaceflight.[3,10,18]

A variety of studies have demonstrated the feasibility of conducting surgical procedures in the simulated microgravity environment and in spaceflight, with most existing and future spacecrafts having sufficient volumes to allow providers to perform procedures.[3,9] Successful procedures in space will require sterile equipment. Although there has been research investigating the microbiome of space and spacecrafts,[1,2,6] this has not focused on in-flight sterilization of the equipment necessary for successful execution of invasive medical and surgical procedures.

The ability to sterilize instruments is crucial in preventing surgical site infections and other life-threatening surgical and postsurgical complications, such as microbial contamination and disease transmission.[12] This is likely to be just as true in space as it is on Earth.[16] Even storing instruments outside the habitat may not be sufficient since bacterial spores have been shown to survive in space.[5] Traditional autoclaves weigh up to

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454 kg and can be very large, some comparable to the size of a semitruck or airplane.[19] A medical grade autoclave can use up to 300 gal of water a day and up to 222 kW/day during high-usage periods.[17] Given the habitable volume limits of space vehicles and the energy requirements of lifting mass into space, mission planners must carefully ration the available mass, volume, and energy expenditures of the spacecraft. This is especially true in the packaging of additional contingency equipment (such as those used to treat unplanned health incidents) which should be small and light enough to not interfere with crucial mission objectives and equipment.

One solution is to hold high-mass equipment in digital stasis using weightless electronic files, which can be converted into physical instruments and equipment using three-dimensional (3D) printers. This allows a limited mass of material to be converted to a variety of purposes on demand. On missions with small crews, limited resources, and tight timelines, one must also consider the operating cost of the medical system for aspects of the mission itself.[13] The primary advantage of 3D-printing for space missions is localized manufacturing.[6] It appears to be a promising modality to provide surgical resources in space and other remote environments.[21] 3D-printing can be used to turn weightless electronic files into surgical and medical instruments that can be safely used during spaceflight. In addition, 3D-printer filament can be recycled and reused, allowing a limited supply of filament to be even more useful.[14] 3D-printed products are reusable and can be used on-demand. Their ability to be regenerated is cost-effective and provides an environmentally friendly edge, while their ability to be used on-demand increases accessibility and time-efficiency.

3D printers have been successfully used in space and are a promising technology to enable crews to "carry" contingency equipment, such as spare parts and medical instruments, without sacrificing critical mass and volume needed to support the primary mission objectives. This paper demonstrates that this technology can be applied to sterilization equipment and provides a digital template for such equipment. In 2014, from a collaboration between NASA and Zero-G technology, a 3D printer was used for the first time to successfully print an object aboard the microgravity environment of the International Space Station, using ground controllers to send and adjust printing files.[7] This groundbreaking event has opened the door to expand the use of 3D printers into space to create surgical instruments without affecting speed or performance of procedures.[20] Having a 3D-printing device that can function in the conditions of space and create its own maintenance parts, surgical equipment, and a machine that can sterilize those instruments will revolutionize medical treatment in space as it creates an endless reservoir of supplies. Many limitations of medical care in space, such as malfunctioning parts or contaminated fields/tools, would be eliminated, thus allowing for timely medical care and treatment. Its portability, ability to be controlled remotely, and localized and additive manufacturing gives 3D printers a primary advantage over other modes of engineering both for medical and nonmedical needs during spaceflight.

METHODS

A portable sterilizer, shown in **Fig. 1**, was developed for use with far ultraviolet-C (Far UV-C) light-emitting diode (LED) lights during spaceflight with Autodesk Fusion 360 and printed with polylactic acid filament to provide stability and durability. The device includes a base, rear support post, and an overhang on which the Far UV-C LED lights are placed. These lights, when activated, illuminate the surface of the base, thus sterilizing any instrument that is placed on it. Objects required beyond polylactic acid filament (1 kg, 160 in^3) include the 3D printer itself (7.3 kg, 738 in^3), 15 Far UV-C LED lights, solder lead, wire, and a flux pen with soldering station. Following 3D-printing of the sterilizer, the Far UV-C LED lights will need to be assembled to the inside of the overhang using the solder lead, wire, and flux pen from the soldering station. If soldering is not feasible, Far UV-C LED lights with wire legs can be used in assembly with the wire. The total mass and volume required to store this equipment prior to assembling is approximately 19.8 kg and approximately 5.9 ft^3, respectively. Following assembly, the overall height of the sterilizer is 4.0 in. The overall length is 8.0 in. The overall width is 5.0 in. The height of the overhang is 1.0 in, and the height of the rear support post is 2.0 in. The height of the base is 1.0 in, and the width of its side is 0.5 in. The height of the sides of the base is 0.5 in.

The 3D-printed portable sterilizer was tested against Clorox Disinfecting Wipes, a leading commercial disinfectant brand, as shown in **Table I**. To assess the sterilizer for its effectiveness in killing bacteria, bacterial swabbing and culture growth on agar plates via incubation was performed.

The study was conducted in a series of three trials, each utilizing a different duration of Far UV-C LED light activation (3 min, 6 min, and 10 min). Each of the three trials was separated into three tests to ensure accuracy and realistic results. The study design included two controls, one of which was the number of

Fig. 1. Original sterilizer 3D-printed via the Autodesk Fusion 360 program.

Table I. Comparison Between Properties of 3D-Printed Sterilizer, a Traditional Autoclave, and Clorox Disinfecting Wipes.

DEVICE	MASS (kg)	VOLUME (ft^3)	POWER REQUIRED (kw)	EFFICACY	LIFESPAN (yr)
3D-Printed Portable Sterilizer	0.32 (fully assembled)	0.09	∼0.038	Sterilization of bacteria up to 100% within 10 min	∼36
Traditional Autoclave	∼500	Up to 200	∼30	Sterilization of microorganisms up to 100% within 6 min	30+
Clorox Disinfecting Wipes	∼2.6	0.20	None	Disinfection of viruses and bacteria up to 99.9% within 10 s	1

bacterial colonies on the surface of the sterilizer base without having activated the Far UV-C LED lights. The second control was the percentage of bacterial colonies killed from the surface of the sterilizer base after applying Clorox Disinfecting Wipes. This percentage was obtained by initially swabbing the surface of the sterilizer base and incubating a petri dish with agar of the sample in an incubator at 37°C. Once incubated for 48 h, the colonies grown on the dish were counted using ImageJ and recorded. This process was repeated after Clorox Disinfecting Wipes were used to clean the surface of the sterilizer base, and the colonies grown on the dish were counted using ImageJ and recorded. These values, obtained before and after applying Clorox Disinfecting Wipes, were used to calculate a percentage of bacteria killed, thus determining the effectiveness of the Clorox Disinfecting Wipes for that trial.

The rest of the trials consisted of recording the number of bacterial colonies on each dish before and after activating the Far UV-C LED lights for a total of 3 min, 6 min, then 10 min. These numbers obtained were converted to percentages of change to best depict the effectiveness of the sterilizer at various durations of application.

RESULTS

Our results in **Fig. 2** showed that Clorox wipes, when used as a sterilizing agent during three different trials, had a percentage change of 99.37%, 75.86%, and 100% when measuring residual bacterial growth, with an average kill percentage of 91.54%. When using Far UV-C LED lights as a sterilizing agent for a period of 3 min, it had a percentage change in bacterial growth of 97.37%, 100%, and 99.16% when measuring residual bacterial growth, with an average kill percentage of 98.84%. When using Far UV-C LED lights as a sterilizer for a period of 6 min, it had a percentage change of 100%, 100%, and 97.23%, with an average kill percentage of 99.08%. When Far UV-C LED was allowed to operate for 10 min, the percentage change was noted to be 100%, 100%, and 100%, with an average kill percentage of 100% [analysis of variance $P < 0.0001$, degrees of freedom 14 (between groups 4; within groups 10)].

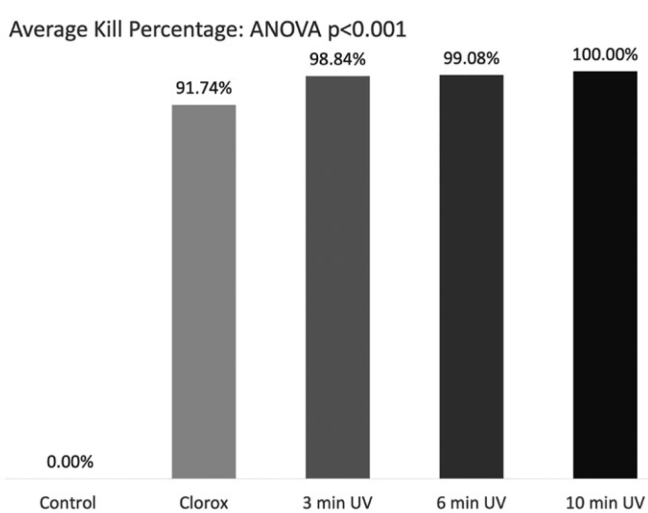

Fig. 2. Average kill percentage of controls and each UV duration.

DISCUSSION

To address the need for a low-mass, low-volume, energy-effective, and accessible medical sterilization instrument in space, we have designed and tested the efficacy of a 3D-printed sterilizer in eliminating bacteria that could otherwise be harmful to spacecraft crew members. This sterilizer, in contrast with a traditional autoclave, only requires 0.038 kW of electricity to function. Its mass and volume are 0.032 kg and 0.09 ft^3, respectively. The minimal weight and size of the sterilizer allow for convenient application in spaceflight. Sterilization, as opposed to disinfection, completely eliminates all forms of microbial life, whereas disinfection eliminates vegetative forms of microorganisms with the exception of bacterial spores from inanimate objects.[15] Medical devices that enter sterile environments, such as surgical tools, need to be sterilized, rather than simply disinfected by means of disinfectant wipes/solutions. Additionally, this portable sterilizer proposes more value than sealed, presterilized equipment,[11] as it allows for repeated use in both a time- and resource-conservative fashion while still maintaining a high level of sterilization.

With the continued advancement in space technology, spaceflight missions are becoming longer and humans are traveling further from Earth. With this, the odds of running into a medical emergency that may warrant surgical intervention increase. Prior studies have shown both the spatial[8] and technical feasibility to perform surgery in space. We aimed to demonstrate that proper sterilization can also be adequately executed in a cost-efficient, timely manner using a 3D-printed device. Our sterilization device was able to kill 100% of bacteria after 10 min. The lifespan of the LEDs allows for approximately 52,560 sterilization cycles. Assuming the sterilizer is used to conduct 4 sterilizations per day, every day, its lifespan will last 36 yr. These results show the viability of a 3D-printed device and associated electrical components to help crewmembers eliminate potentially harmful bacteria from medical and surgical instruments for time-sensitive operations and procedures in space.

There are several limitations worth noting. First, the data collected was not bacteria-specific and did not test the effectiveness of the sterilizer on spores, fungus, or viral pathogens. Future studies with this device will need to investigate its effectiveness against spore-forming bacteria and other pathogens known to be a risk in spaceflight. Another practical consideration is that we did not test the sterilizer in microgravity. Related to this is the need to confirm that the device itself could be printed in microgravity since the absence of a constant directional force can interfere with the structural integrity of items being printed. Further, it is important to consider the number of UV LEDs in relation to efficiency. While this study was conducted using 21 LEDs and obtained 100% effectiveness within 10 min, additional testing could be done with increasing and decreasing the number of LEDs used to determine if there is a correlation between the number of LEDs and duration of time it takes to obtain a 100% disinfection rate and thus improve cost and efficiency. It is also unclear whether this sterilizer would be effectively able to sterilize instruments with crevasses or channels where the UV light would not effectively penetrate and is another area that could be further tested.

In conclusion, we have successfully demonstrated on a small scale the ability to create a device using 3D-printing and UV LEDs that can effectively sterilize surgical instruments. This device could easily be made in situ on a spacecraft with minimal upmass, allowing the performance of sterile surgical procedures to take place within a spacecraft environment. Future work will focus on addressing the limitations outlined above.

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Aerospace Medicine Clinic

This article was prepared by Caleb S. James, D.O., M.P.H.

You are seeing a 21-yr-old air traffic controller who is taking 50 mg bictegravir, 200 mg emtricitabine, and 25 mg tenofovir for a diagnosis of human immunodeficiency virus (HIV). He presented to an urgent care facility 16 mo ago with full-body rash, fever, body aches, enlarged lymph nodes, and lesions on his genitals. His initial screening for HIV was positive as were labs for herpes and syphilis. He was treated for early syphilis with a one-time dose of 2.4 million units of penicillin G with appropriate response of his rapid plasma reagin (RPR) titers from 1:32 to 1:2. The Centers for Disease Control and Prevention (CDC) recommends this dosing and treatment for primary and secondary syphilis regardless of HIV status.[6] Confirmatory HIV testing returned positive the following week. He was evaluated by an infectious disease specialist, who determined he was stage 1 by CDC criteria with a CD4 of 723 cells · μL^{-1} and viral load of 38,243 copies · mL^{-1}.[2] Labs drawn 2 mo after initiating antiretrovirals showed a viral load of 30 copies · mL^{-1}, CD4 of 648 cells · μL^{-1}, and RPR titers of 1:32. His HIV viral load has been undetectable on testing every 3 mo since that time and he has had no other syphilis testing. He has no history of acquired immunodeficiency syndrome-defining illnesses, no longer engages in high-risk sexual activities, denies any illnesses since initiating antiretroviral therapy, and has taken no antibiotics since his initial diagnosis. Positive findings on physical examination include diffuse hyperreflexia of the upper and lower extremities, slightly decreased proprioception of the left great toe, and several beats of clonus at each ankle.

1. What is the most concerning finding on review of his history?
   A. His CD4 count decreased from 723 to 648 cells · μL^{-1}.
   B. Enlarged lymph nodes were observed on initial presentation.
   C. Secondary syphilis should be treated with 2 wk of antibiotic therapy.
   D. RPR titers went from 1:2 to 1:32 on repeat testing and he has taken no antibiotics.
   E. The infectious disease specialist placed him in HIV infection stage 1 by CDC criteria.

ANSWER/DISCUSSION

1. D. The patient's RPR titers showed appropriate response from 1:32 to 1:2 after he was treated for what was believed to be early syphilis 16 mo ago. However, the follow-up labs 2 mo after treatment showed a return to 1:32, which indicates reinfection or treatment failure. He reports no history of further treatment or new illnesses/symptoms. Therefore, he likely now has late latent syphilis. It is also concerning that he has neurological findings on clinical examination. His CD4 count did decrease slightly, but it remained greater than 500 cells · μL^{-1}, which continues to meet HIV infection stage 1 by CDC criteria.

Your concerns prompt consultation with an infectious disease specialist, who agrees with your assessment. The CDC recommends a single intramuscular dose of 2.4 million units of benzathine penicillin G for those with early latent syphilis, but three intramuscular doses of 2.4 million units of benzathine penicillin G given at 1-wk intervals for those with late latent syphilis.[6] As this individual's titers reverted more than 12 mo ago, this represents late latent syphilis.[3] While the patient denies any recent illnesses, memory issues, or motor/sensory dysfunction, the specialist also concurs that the neurological findings on examination raise suspicions for neurosyphilis in the setting of treatment failure. Due to these concerns, the specialist recommends a lumbar puncture to assess for evidence of *Treponema* in the cerebrospinal fluid. The patient undergoes lumbar puncture, and the cerebrospinal fluid shows no evidence of infection. Therefore, you begin a workup for hyperreflexia and all labs return within normal limits, except for a low-normal vitamin B12. You decide to obtain magnetic resonance imaging of the spine but must determine the most likely location for a lesion to appropriately target the imaging.

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2. If a spinal cord lesion were causing this individual's neurological findings, where would you expect the lesion to be located?
   A. C3-4.
   B. T3-4.
   C. T6-9.
   D. T12-L1.
   E. L5-S1.

ANSWER/DISCUSSION

2. A. Diffuse hyperreflexia in the upper and lower extremities indicates a lesion above the level of the hyperreflexia. As the individual had hyperreflexia to the bilateral upper and lower extremities, C3-4 is the most likely of the above choices in this individual. While clonus was only noted in the lower extremities, other commonly tested clonus reflexes include masseter, patellar, biceps, and triceps.[13] Ultimately, the patient was found to have a syrinx located at C3 on magnetic resonance imaging that was thought to be too small to cause his symptoms. It was also not thought to be secondary to his diagnosis of HIV or late latent syphilis. Interestingly, his hyperreflexia and clonus resolved after treatment of late latent syphilis, raising the possibility that his hyperreflexia was, in fact, a subtle sign of neurosyphilis. However, it is also possible that the hyperreflexia was due to increased sympathetic tone, as he was nervous on initial examination, day-to-day variation in this individual, or another cause. You recommend that the patient begin taking vitamin B12 supplementation and follow up with his primary care manager. Given the individual's concerns for the return of his syphilis diagnosis, he asks if there is a testing schedule that he should follow to ensure his current course of antibiotics effectively treated his diagnosis of late latent syphilis.

3. Given the patient's history, what is the most appropriate schedule to perform monitoring for response to treatment for late latent syphilis?
   A. 3, 6, 9, 12, and 24 mo.
   B. 6, 12, and 24 mo.
   C. 3, 12, and 24 mo.
   D. 6, 18, and 36 mo.
   E. 6 and 12 mo.

ANSWER/DISCUSSION

3. B. The schedule for monitoring treatment response for late latent syphilis with a quantitative nontreponemal serologic test is the same for both HIV-positive and HIV-negative individuals: 6, 12, and 24 mo.[4] In HIV-positive individuals with primary or secondary syphilis, the schedule for assessing treatment response is 3, 6, 9, 12, and 24 mo.[6] Individuals diagnosed with primary or secondary syphilis who have no history of HIV should undergo serologic testing at 6 and 12 mo.[5] Now that his late latent syphilis has been managed, you can begin to discuss the aeromedical risks of HIV with him, which include development of progressive immunodeficiency, neurocognitive dysfunction, and adverse effects related to his antiretroviral therapy. You explain that progressive immunodeficiency is unlikely if he maintains excellent medication adherence and that current regimens do not have the same profile of significant side effects that older antiretroviral medications had. However, you inform him that HIV-associated neurocognitive disorder (HAND) has been reported in individuals who have no detectable viral load and are otherwise healthy. Overall incidence of HAND in several large studies ranges from 14–52%.[1] Cognitive changes associated with HAND could include executive dysfunction, memory impairment, and loss of impulse control. More subtle impairments could include compromise in cognition, motor function, and behavior.

4. How frequently would the Federal Aviation Administration (FAA) require him to undergo neuropsychological testing to ensure that he has no detectable neurocognitive declines?
   A. Every 3 mo.
   B. Every 6 mo.
   C. Every 12 mo.
   D. Every 24 mo.
   E. Every 36 mo.

ANSWER/DISCUSSION

4. C. First- and second-class airmen with HIV require neuropsychological evaluation annually, whereas third-class airmen require testing every other year.[8] After educating him on the FAA timelines, he asks if there is anything he can do to prevent progression to HAND. He states that both parents have a history of diabetes. His father has a history of alcohol abuse and his mother has a history of hypertension and hepatitis C. He states that he will strictly adhere to his medication regimen, maintain a monogamous relationship with his fiancé, and always wear condoms. You inform him that while he could progress to HAND unexpectedly, there are several factors that increase the risk.

5. Of the diagnoses in his family history, which of the following increases the risk of HAND?
   A. Diabetes.
   B. Hypertension.
   C. Hepatitis C.
   D. Substance abuse disorders.
   E. All of the above.

ANSWER/DISCUSSION

5. E. Medical comorbidities, coinfection, substance abuse disorders, psychopathology, and socioeconomic factors have been tied to the development of HAND in medical literature.[12] The patient's age makes it difficult to determine the likelihood to progress to HAND, as the CHARTER and POPPY studies had an average age of 40–50 yr.[7,9] Also, individuals in these studies had to take antiretroviral medications that had more significant side-effect profiles than those that are presently used for treatment. The aeromedical concerns in this individual regarding HAND are subtle decrements that are imperceptible to him or others that could cause lack of attention to detail or inability to multitask.

None of the military branches recommend waivers for untrained assets. The Army considers waivers on a case-by-case basis for initial applicants for classes 2, 3, and 4 and all classes for trained individuals*; the Air Force considers waivers for flying classes II and III, Air Traffic Control, Ground Based Operators, and Special Warfare[10]; and the Navy considers waivers on a case-by-case basis for classes II, III, and IV.[11] Aviation Medical Examiners must defer to the FAA.[8] All military branches and the FAA require neuropsychological testing to be performed prior to waiver consideration.

The individual's syphilis was treated to resolution with no recurrence and no neurological sequelae. He continues to practice safe sex with strict adherence to condom use and his viral load is currently undetectable. He strictly adheres to his medication regimen and will be followed at regular intervals to ensure no subtle neurocognitive deficits.

James CS. *Aerospace medicine clinic: late latent syphilis in the setting of human immunodeficiency virus*. Aerosp Med Hum Perform. 2023; 94(11): 861–863.

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Aerospace Medicine Clinic

This article was prepared by Isaac Yourison, M.D.

You're the senior flight surgeon on call in the Medical Group when your nurse runs into your office and proceeds to rapidly tell you about a patient who just called the advice line. He is a 45-yr-old, right-handed, male squadron commander in the Air Traffic Control Wing. His wife woke him around 3:30 this morning to see why the dog was barking. He went downstairs and found the dog barking at something outside. He flipped on the flood light and pushed the curtain to the side, which is when he realized he couldn't feel the curtain with his right hand. This did not strike him as odd, since he thought his arm may have just fallen asleep. Of note, he and his daughter had a conversation about the dog barking and she didn't mention that he had slurred or confused speech. He went back to bed and noticed that he moved his phone on the nightstand by brushing the charging cable and became concerned as his sensation had not returned. He went to his wife's powder mirror and didn't notice any facial droop, but did feel his upper lip was numb on the left more so than the right. He went back to bed but was unable to get to sleep because he was feeling anxious.

Waking up later around 5 a.m., he got out of bed and performed his morning routine, which included brushing his teeth and shaving with his right hand. He noticed that he had to be very intentional about how much pressure he was applying to the toothbrush and razor as well as his teeth and face. He felt he had to consciously tell himself to push harder or lighter with his right hand. He drove to work, which is about an hour away, and began climbing the stairs to his floor. A woman walking up behind noted that he looked pale, which he told her was due to him feeling a bit worn down. He sent some emails stating that he wouldn't be in afternoon meetings, then called a nurse advice line and was routed to you as the flight surgeon on duty. After reviewing the case, you are concerned that he is having an acute ischemic stroke and recommend he go to the nearest emergency room.

1. Which of the following, if present, would exclude him from receiving intravenous tissue plasminogen activator (tPA)?
   A. Onset of symptoms for <4.5 h.
   B. Stroke associated with aortic arch dissection.
   C. Persistent blood pressure (BP) elevation of 175/105 mmHg.
   D. Platelet count 120,000/mm^3.

ANSWER/DISCUSSION

1. B. Stroke associated with aortic dissection is a contraindication to receiving tPA due to the increased risk of brain ischemia from hypotension and direct compromise of cerebral circulation. Onset of symptoms for <4.5 h is an inclusion criterion to administer tPA. Other inclusion criteria include age >18 yr and clinical diagnosis of ischemic stroke causing neurological deficit. BP elevation is not a contraindication unless BP is sustained >185/110 mmHg. Thrombocytopenia is not a contraindication until platelets are <100,000/mm^3.[11]

The patient drove an hour back to his hometown and was evaluated in a local emergency room. Based on his history and exam findings, the physician was also concerned that he was having an ischemic stroke. Vital signs were within normal limits, with the exception of mild hypertension (HTN), BP 148/92 mmHg. Neurological exam demonstrated normal cranial nerves II–XII, with the exception of left lower facial nerve sensory loss in the V2 distribution, normal strength in upper and lower extremities, decreased sensation to light touch on the lateral aspect of his right hand and wrist, normal deep tendon reflexes, normal gait, negative Romberg, no pronator drift, no dysdiadochokinesis, and negative Babinski and Hoffman testing. No aphasia, visual cuts, or gaze preferences were noted on exam. Other medical, surgical, social, and family histories and review of systems were negative and noncontributory. Lab results with complete blood count, basic metabolic panel, and coagulation studies were within normal limits. Coronary lipid panel, thyroid studies, and glycosylated hemoglobin were drawn, but did not return for several days. Initial imaging studies were unremarkable and included noncontrast computed

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tomography of the head, computed tomography angiography of the head and neck, and lower extremity venous duplex. However, magnetic resonance imaging of the brain revealed an acute ischemic stroke in the posterior left middle cerebral artery (MCA) distribution. He was determined not to be a candidate for tPA, since it was >4.5 h after the event. He was transferred to a larger local hospital for acute stroke management. A follow-up echocardiogram with bubble study showed an intracardiac shunt consistent with a patent foramen ovale (PFO).

2. Given the findings presented above, what is the most likely etiology of his stroke?
   A. Large intracranial vessel thrombotic occlusion.
   B. Systemic hypoperfusion.
   C. Cardioembolic.
   D. Blood and hypercoagulable disorder.

ANSWER/DISCUSSION

2. C. As the PFO is the likely source of the stroke, the most likely etiology is cardioembolic. At the time of his stroke, his Risk of Paradoxical Embolism (RoPE) score was 8, which suggests an 84% chance that his stroke was due to the PFO and is also associated with a 6% 2-yr risk of recurrent stroke or transient ischemic attack (TIA).[3,8] In the setting of embolic infarct with no other evidence for a source, it is reasonable to conclude that the PFO was the likely mechanism. The RoPE calculator assigns points for HTN, diabetes mellitus, prior stroke, infarct on imaging, smoking, and age. He only received points for cortical infarct on imaging. His condition stabilized in the hospital, and he was started on a statin and dual-antiplatelet therapy and instructed to follow up with Cardiology and Neurology. His lip symptoms resolved within 2 d and his hand symptoms within 1 wk. At his outpatient Cardiology follow-up appointment, the results of his workup, including complete blood count, basic metabolic panel, glycated hemoglobin, thyroid-stimulating hormone, and a thorough hypercoagulable panel, were noted to be within normal limits. His lipid panel revealed a low-density lipoprotein level of 135. A follow-up lipid panel 2 mo later showed an appropriate decrease in low-density lipoprotein to 64. He underwent a 48-h Holter study and results were read as normal. He was determined to be a good candidate for PFO device closure and underwent successful closure of the PFO with a St. Jude Amplatzer™ device (Abbott Laboratories, Chicago, IL) in the following weeks. Aspirin and clopidogrel were continued for 6 mo. Clopidogrel was stopped after 6 mo and he was continued on atorvastatin and baby aspirin. A medical evaluation board was submitted, and he was found suitable for continued military duty.

Today he comes to see you at the flight surgeon's office to discuss a possible aeromedical waiver and return to air traffic control (ATC) duties, as he is approximately 12 mo status post his cerebrovascular accident. Per Air Force regulations, stroke and TIA are disqualifying for all flying classes.[7] Congenital cardiac anomalies are also disqualifying, specifically PFO associated with embolic phenomena. Waivers are generally not considered unless a correctable cause is discovered and treated. Since in this case a correctable cause (PFO) was successfully treated, ATC waiver is possible. He is very motivated to return and wants your opinion on future risks.

3. In addition to recurrent stroke, what are the other related events of aeromedical concern if he returns to duty?
   A. Myocardial infarction.
   B. Seizure.
   C. Aphasia.
   D. Fall risk.

ANSWER/DISCUSSION

3. B. Aeromedical concerns after stroke are future risk of seizure, risk of stroke recurrence, and residual neurological or cognitive deficits. Regarding seizure, which could lead to sudden incapacitation, the risk is more elevated within the first year after stroke. Based on his SeLECT score of 3, his risk of seizure within the first year was 4%.[6,9] The SeLECT calculator assigns points for severity of stroke, large-artery atherosclerotic etiology, early seizures, cortical involvement, and territory of MCA involvement. He received points for cortical and territory of MCA involvement. There is also an additional 2% risk over the following 4 yr, so his annualized risk of seizure is 0.5%. Regarding recurrent stroke, which could cause either immediate incapacitation or decrements, his Essen stroke risk score (based on prior stroke, age, history of diabetes mellitus, HTN, myocardial infarction, smoking, or atherosclerotic cardiovascular disease) estimates his 1-yr risk of stroke at 1.8%.[13] However, this does not account for his PFO or subsequent closure, so the exact risk is more difficult to determine. Regarding residual neurological deficits, the risk is not easily quantified. The potential for recrudescence exists after infarction of brain or spinal cord tissue and would likely present in a similar fashion to his original cerebrovascular event but would not be expected to be incapacitating.

4. While PFO device closure can reduce stroke risk, it can be prone to adverse events. What is a feared complication from a PFO closure device that could also increase stroke risk?
   A. Atrial fibrillation (AF).
   B. Device migration.
   C. Cardiac erosion.
   D. Allergic reaction.

ANSWER/DISCUSSION

4. A. AF related to device implantation can increase stroke risk and is more common in PFO patients who had percutaneous closure compared with those who are medically treated. The risk of AF is higher in the first 45 d postclosure, up to a rate of 3.7 patients per 100 patient-years.[2] This can be up to five times the level of medically managed patients but decreases with time. Cardiac erosion is also a feared complication from PFO closure but is not necessarily linked to increased stroke risk. The best estimate for incidence of erosion with the St. Jude Amplatzer device is 1–3 cases per 1000 implants (0.1%),[1] but this can lead to significant mortality when it occurs. Device migration and allergic reaction are less likely and not known to be related to stroke risk. You discuss with the patient that he should seek immediate medical attention for any palpitations, chest pain, dizziness, or collapse. Regular echocardiographic follow-up to ensure absence of pericardial effusion, alteration in device position, or other abnormalities is recommended.

The patient is doing well and asks what the next step is for aeromedical waiver submission. He undergoes repeat physical exam, with no signs of neurological deficits on routine exam or on neuropsychological testing. There are no indications that he has residual cognitive deficits from his stroke. You discuss that per the U.S. Air Force waiver guide, "supratentorial strokes leave a potential seizure focus. A 2–3-yr seizure-free observation period after stroke and a 1–2-yr observation period after TIA are required prior to any potential waiver consideration."[7] He has had no seizures or further events and is approaching his 2-yr window, so you draft and submit his waiver.

5. The patient asks you what would have happened if he had been a civilian aviator/controller or had been serving in another branch of the military. You immediately pull up your Federal Aviation Administration (FAA) Guide for Aviation Medical Examiners, which is saved in your browser, and answer that it would most likely have led to:
   A. Immediate disqualification.
   B. No change in status.
   C. Discharge from service.
   D. Unknown status.

ANSWER/DISCUSSION

5. A. Per the FAA's Guide for Aviation Medical Examiners, stroke is disqualifying and requires an FAA decision before an individual can be granted a Special Issuance and subsequent medical certificate.[5] The other branches of the military have similar standards. Per Navy guidelines, TIA and/or stroke are permanently disqualifying and waiver approval is deferred to the Naval Authority.[10] Army standards offer similar guidance, since stroke does not meet the standards of medical fitness for flying duty.[12] Your patient is considering working in the civilian sector after his retirement, and since civilian-contracted ATCs must hold a current 2nd class FAA medical certificate,[4] he will keep the regulations in mind when transitioning out of military service.

After an evaluation of his records, he was recommended for a flying class III/ground-based operator/ATC waiver, valid for 2 yr. The Aeromedical Consultation Service recommends reevaluation with repeat echocardiograms every 3 yr. He returns to duty after his waiver approval and continues to follow-up closely with you until you are given orders for permanent change of station.

Yourison ID. *Aerospace medicine clinic: stroke*. Aerosp Med Hum Perform. 2023; 94(11):864–867.

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The History of Surgical Care in Space Symposiums

Mark R. Campbell

Over the last 40 yr, NASA has sponsored a series of symposiums dealing with the issues of surgical care during spaceflight (**Table I**). This article briefly summarizes those workshops and highlights the changing thought processes of the participants. It is interesting to note that the issues and questions to be resolved are essentially the same from symposium to symposium, but both the questions and the conclusions have become more sophisticated over the years.

Conceptualization and Planning Symposium for the Management of Trauma and Emergency Surgery in Space—July 20–21, 1983, Houston, TX[16]

The design reference mission was a space station with a small definitive medical care time (14–21 d predicated on the Shuttle flying every 2–3 wk) that would be self-sufficient regarding medical and surgical care. Many issues were discussed by the 20 academic surgeons who attended, including chest trauma, vascular trauma, abdominal trauma, orthopedic injuries, neurosurgical trauma, burns, postoperative care, monitoring, anesthesia, diagnostic radiological imaging, medical computer data management, and surgical training for a future space surgeon.

Full surgical capabilities were advocated. Less than that was considered "foolhardy and unacceptable." A fully trained general surgeon actively practicing clinical surgery was advocated as the crew medical officer (CMO). The main technical problems identified were restraint and the control of bleeding in weightlessness. Animal surgery in parabolic flight was advocated to gain experience with surgical techniques in space. It was advocated that a consultant's network be established and used on a regular and continuing basis. Telemedicine experience needed to be developed.

In retrospect, the conclusions seem naive. However, this is more understandable given the extreme optimism at this time regarding future spaceflight, as the Shuttle would be flying every 2–3 wk and we would soon be building a large space station.

Space Station Freedom Health Maintenance Facility Consultants Conference (Surgical Care Issues Working Group)—August 27–29, 1990, Houston, TX[2]

The purpose of this multispecialty medical conference was to discuss the evolving capabilities of the proposed Space Station Freedom health maintenance facility (HMF), especially in light of recent mandated changes in downsizing the facility. The Space Station Freedom project was active from 1984–1993 and was different from the International Space Station (ISS) in that there was not a medical evacuation option [no Soyuz or assured crew return vehicle (ACRV)]. Therefore, it had a definitive medical care time of 45 d (time required for Shuttle rescue). The medical care system needed to be very surgically capable, and this was provided by the HMF. The CMO would probably be an M.D., and some were still advocating a surgeon. The HMF was 1200 lb and 2400 ft^2.[1,3] It consisted of a surgical workstation (waist-level operating room table), digital X-rays, surgical task lighting, surgical cautery, ventilator, defibrillator, intravenous pump, a waste management system (including surgical suction), a medical computer, capability for telemedicine, and anesthesia.[15] Surgical procedures being proposed were complex wound closures, chest tube insertion, tendon repair, appendectomy, limb amputation, orthopedic procedures, and open abdominal, thoracic, and vascular procedures.

The following changes had recently been mandated for the HMF just prior to the conference:

- An ACRV would probably be present, providing a medical evacuation option;
- The digital X-ray capability would be eliminated;
- Surgical cautery had a radio frequency interference problem and would be eliminated;
- The waist-level workstation (operating room table) was in doubt due to too much weight and volume;
- The CMO would probably not be an M.D.; and
- There was an overall need to greatly decrease weight, volume, and power.

The capability to perform open abdominal procedures, vascular procedures, thoracic procedures, and the treatment for all except minor burns needed to be dropped. The need to perform advanced trauma life support (ATLS) was still critical—cervical collar and pelvic binder use and chest tube insertion were emphasized. The capability to perform open orthopedic procedures needed to be dropped. Most fractures could be treated with splinting or relatively simple external fixation. There was a critical need for X-ray

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Table I. Surgical Care in Space Symposiums.

DATE	TITLE
1983	Management of Trauma and Emergency Surgery in Space
1991	Space Station Freedom HMF Consultants Conference (Surgical Care Issues Working Group)
1996	Life Sciences Long-Duration Spaceflight Conference
1997	Clinical Capabilities Development Project—Surgical Care Issues Working Group
2002	Long-Duration Mission Surgical Planning Working Group (Dr. Norm McSwain)
2005	Surgical Science in Support of Human Space Exploration
2015	National Space Biomedical Research Institute Surgical Capabilities for Exploration
2018	Minimally Invasive Expeditionary Surgical Care Using Human-Inspired Robots

capability, as there was no realistic ability to accurately diagnose a pneumothorax. However, many in the group felt that a pneumothorax could be diagnosed and treated based upon clinical findings. Orthopedic injuries could be adequately diagnosed and treated without X-ray capability. Ultrasound had a future potential that was very promising for a wide range of imaging situations.

There was a concern about delayed wound-healing during spaceflight. The wound-healing ability during spaceflight was unknown. There was a concern about bleeding, restraint, and surgical performance in weightlessness. It was unknown if these issues were problems, as no experience existed. Parabolic flight research could answer some of these questions. There was a concern about contamination of cabin atmosphere with biological fluids. Containment surgical hardware might be needed. Most agreed that efforts should continue to have the CMO be an M.D. The statement was made, “Don’t put hardware onboard unless you have the CMO capability to use it. Limitations will be based upon the CMO capabilities and not the hardware.”

In summary, with the need to downsize the HMF and the presence of an ACRV for medical evacuation that would decrease the definitive medical care time to 24 h, the surgical capabilities required were greatly reduced. There was a more realistic connection between what capabilities were absolutely needed and the severe operational constraints defined by the minimal hardware provided and the limited training of the CMO. Areas where we had a lack of knowledge or experience on how to actually perform a surgical procedure in weightlessness were better defined. In the next several years following this symposium, a series of parabolic flights were performed that helped to answer procedural questions regarding surgery in weightlessness, such as how to provide restraint,[9] how to control bleeding,[7] the difficulties in performing a complex surgical procedure,[6] and the feasibility of performing ATLS procedures.[8]

Clinical Capabilities Development Project—Surgical Care Issues Working Group—April 8, 1997, Houston, TX

This multispecialty medical conference mostly focused on the ISS, but issues concerning future long-duration spaceflight were also discussed. There were several important changes to the space station project. The Space Station Freedom was now the ISS and the HMF (1200 lb) was now the health maintenance system (200 lb). The waist-level workstation was now a floor-level crew medical restraint system. There would be a medical evacuation option (either Soyuz or X-38/ACRV). The CMO would not be an M.D. and would have minimal training (less than 200 h). The health maintenance system was capable of advanced cardiovascular life support and ATLS except for no chest tube insertion hardware or training. It had a ventilator, monitor, and defibrillator. The focus was on stabilization, monitoring, and transport. There was no integrated surgical kit and there was no ability to organize and restrain surgical instruments. Surgical instruments were provided in individual sterile packaging only.

The most important life science issues for future long-duration spaceflight were felt to be: psychological support; radiation effects; cardiac, bone, and strength deconditioning; and providing for remote medical/surgical care. The surgical issues that were discussed included laparoscopy,[5,11] future robotic surgery, CMO capabilities (hopefully an M.D.), prophylactic appendectomy,[10] extremely long communication delay with telemedicine, delayed wound-healing, and future blood substitutes. It was stated, “There is not any operation performed laparoscopically that cannot be performed easier and with less hardware as an open procedure.”

Long-Duration Mission Surgical Planning Working Group—October 2002, Houston, TX

This was chaired by Dr. Norm McSwain and, unfortunately, there are no published results. The group consisted of 20 academic leaders in surgery and critical care medicine who were generally not familiar with space medicine. The group was given a Mars expedition as a design reference mission and discussed what surgical events would need to be treated and what should be the expedition medical officer’s (EMO) credentials and training. The goal was to develop a detailed training curriculum.

The surgical capabilities need to be selected based upon:

- High incidence of occurrence;
- High impact to mission or crewmember;
- High ability that treatment will result in a curative result;
- Minimal hardware logistics; and
- High ability to be able to train an EMO.

It was concluded that there was a need to have enough surgical capability to perform major open procedures (exploratory laparotomy and appendectomy) and external fixation for orthopedic fractures. Some surgical diseases cannot be treated (vascular surgery is not trainable). Laparoscopy will probably not be available due to hardware constraints and inability to train. Many procedures can be performed with imaging and percutaneous techniques. There was a need to have the capability (hardware, supplies, EMO training) to perform a large number of surgical procedures on future long-duration spaceflights, including, but not exclusively, an appendectomy. An EMO would need training in other fields than surgery, but an M.D. could perform a large number of selected operations at the level of a second-year surgical resident if given 6 mo of focused surgical training.[4]

Surgical Science in Support of Human Space Exploration—December 2005, Houston, TX

This conference was held with 20 mostly academic surgeons familiar with space medicine issues. Discussed topics included robotic surgery, laparoscopy, urological ureteral stenting for stone disease, ultrasound-directed percutaneous drainage,[18] and diagnostic ultrasound to detect pneumothorax and intra-abdominal trauma.[14,17]

Surgical Capabilities for Exploration and Colonization Space Flight—December 2015, Houston, TX—National Space Biomedical Research Institute[13]

This was a multispecialty conference with mostly attendees from surgical fields. All were familiar with space medicine issues.

The issues discussed were:

- Selection of the healthcare provider (CMO);
- CMO training requirements;
- Establishing a controlled healthcare procedure zone in the spacecraft;
- Wound-healing and hemostasis;
- Developing onboard fabrication capabilities (three-dimensional printing of surgical instruments);
- Multitasking of onboard equipment;
- Identifying new healthcare equipment, devices, and supplies; and
- The need for increased resources for research to develop space healthcare devices and supplies.

Minimally Invasive Expeditionary Surgical Care Using Human-Inspired Robots—October 2–3, 2018, Pensacola, FL[19]

This was a narrowly focused discussion group of 25 participants with expertise in robotic design, space medicine, or robotic surgery. It was to familiarize the group with what research potential existed for future robotic surgery in spaceflight.[12]

Conclusion

These conferences and symposia over 40 yr have continually discussed what surgical capabilities would be required for a future long-duration spaceflight and, based upon that determination, what surgical hardware would have to be provided and what level of training would be needed for the CMO. Experience has shown that whatever surgical hardware and CMO capabilities are requested and planned for are drastically diminished by the reality of severe hardware and training constraints.

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NOVEMBER 1998

Current aeromedical risks in U.S. military aviation – Army: (USA Aeromedical Research Laboratory, Fort Rucker, AL): "30% of class A to C accidents involved SD as a significant factor, while…78% of aircrews have been disoriented… [There was] a significant increase in SD associated with combat operations… 90% of the reviewed accidents were thought to involve type I (unrecognized) SD compared with only 43% of the reported incidents; both pilots in a particular aircraft were considered to have been disoriented in at least 59% of accidents compared with 23% of incidents; sudden loss of visual cues… accounted for 25% of SD accidents compared with 13% of incidents; and 62% of the accidents occurred at night compared with only 36% of incidents."[1]

Navy: (Naval Operational Medicine Institute, NAS Pensacola, FL): "[A]ll aviation personnel with a diagnosed personality disorder or those with maladaptive personality traits that have had a documented effect on safety of flight, crew coordination, or mission completion, are determined to be Not Aeronautically Adapted (NAA)… NAA dispositions were made on the basis of personality disorders and maladaptive personality traits in 29% and 35% of the cases, respectively… Obsessive-compulsive features were present in 58% of officer and 10% of enlisted NAA dispositions. Dependent and avoidant features were present in excess in comparison to psychologically healthy aviators, suggesting the incompatibility of these features with aviation."[3]

Air Force: (USAF School of Aerospace Medicine, Brooks AFB, TX): "Maneuvers found to cause the Push-Pull Effect (PPEM)… were found in 11 to 67% of engagements reviewed, depending on the nature of the training mission, with an overall average of 32%. The PPEMs that were observed contained segments of less than +1 G_z, ranging on average from 0.0 to 0.5 G_z for an average of 3.5 to 5 s duration… PPEMs…represent an operationally significant source of risk for accidents."[6]

NOVEMBER 1973

Human Systems Integration (Department of Physiotherapy, Queensland, Australia): "As part of a project concerned with the determination of arm reach boundaries for placement of manual controls within a cockpit, a questionnaire was distributed to a random sample of Australian male and female pilots of light aircraft… Analysis of the responses revealed that, as well as the discomfort experienced in their accommodation, some pilots have definite reaching problems within their cockpits… The facts which have emerged from the questionnaire analysis indicate that some modifications to the aircraft or to its installations need to be made to ensure the provision of safe restraint for pilots while allowing them to reach all controls."[2]

Flying postmyocardial infarction (Ohio State University, Columbus, OH): "The empirical approach to the problem of the airman with a cardiac disease history has been effective with respect to its selectivity… The accident rate does not appear to have been significantly affected by the policy of allowing selected post-infarction pilots to return to active flying. The problem of determining high-risk from reasonable-risk pilots has not compromised aviation safety or the public interest."[7]

NOVEMBER 1948

Human Systems Integration (Civil Aeronautics Administration): "Aviation medical research interests can be represented as a composite of two major areas, one covering aviation in the armed services, the other civil aeronautics. These areas have a common fiducial point, i.e., the combination of man and the aircraft…

"It is concluded that additional quantitative descriptions of man are required, and that a vigorous campaign must be instituted to indoctrinate the aeronautical engineer in the use of biotechnological data."[5]

Bouncing heads (Aero Medical Equipment Laboratory, Naval Air Experimental Station, Philadelphia, PA): "With the advent of jet planes and other types of highspeed aircraft, additional problems in protecting the human organism from the effects of increased velocities and related phenomena have arisen. One such problem concerns the protection of the heads of airmen, flying jet planes, from what has been termed 'buffeting.'

"Buffeting may occur as a result of such events as accelerated take-offs, violent acrobatic maneuvers or flights through turbulent air. It consists essentially of the pilot's head bouncing against the adjacent canopy, which, in the case of jet planes, is in close proximity to this part of the body. The forces involved in such buffeting have been stated to be from 4 to 5 g during level flight at a low altitude on a hot day. Presumably, the applications of these forces are of very short duration."[4]

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

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Aerospace Medicine and Human Performance

November 2023

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