

Aerospace health and safety: today and the future,

volume II

Edited by

Christopher Scheibler, Mardi A. Crane-Godreau,
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Aerospace health and safety: today and the future, volume II

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Editorial: Aerospace health and safety: today and the future, volume II

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Editorial on the Research Topic

Aerospace health and safety: today and the future, volume II

Aviation is a cornerstone of modern commerce, defense, science, and leisure. In 2024 alone, the world's airlines carried an estimated 5 billion passengers, demonstrating their global importance. Now, we stand at the precipice of a new era. With the rise of commercial civilian spaceflights by companies such as Blue Origin, Virgin Galactic, and SpaceX, the dream of space travel is becoming a reality for non-professional astronauts. However, this expansion into a domain where environmental conditions differ widely from our terrestrial experience presents unprecedented challenges and questions regarding human health and safety.

In this second volume of *Aerospace Health and Safety: Today and the Future*, 12 new publications address complex health and safety concerns for personnel working in the air and in space. These studies can be broadly understood through the key themes of physiological adaptation, mental resilience, occupational health, and advanced diagnostics.

One central theme is the physiological challenge of adapting the human body to extreme gravitational changes. In *Peripheral skin cooling during gravitational challenges in parabolic flight*, Bothe et al. investigated a proof-of-concept experimental model that tested peripheral cooling (PC) as a countermeasure to cardiovascular instability during gravitational shifts. Their preliminary testing shows that heart rate and blood pressure fluctuations were reduced, leading them to advocate for further controlled studies to assess PC as a non-invasive countermeasure.

Optimizing balance and sensorimotor function is equally critical. Two articles in this volume report on adapting training for this purpose. In *The ground reaction force pattern during walking under vestibular-demanding task*, Wang Z. et al. examined changes in ground reaction force (GRF) during normal walking and under sensory-deprived conditions. They concluded that these methods could be used not only to detect changes pre- and post-mission but also to develop specific sensorimotor training programs “aimed at enhancing astronauts’ abilities to navigate unpredictable sensory-conflicted conditions”. Recognizing that anatomical differences may influence outcomes, Zhang et al. explored sex differences. In *The sex effect on balance control while standing on vestibular-demanding tasks*, they reported that since both men and women are included in space programs, “it is

essential to clarify how women differ from men when it comes to balance control.” Their work provides a fundamental reference for studying the vestibular system and designing tailored rehabilitation programs for male and female astronauts.

Beyond physical adaptation, maintaining mental health and peak performance under stress is paramount. In *The effect of Ashtanga-Vinyasa Yoga method on air force pilots’ operational performance*, Santos et al. addressed the importance of “optimizing performance and bolstering physical health and mental resilience” in military pilots. Their manuscript describes a feasibility study of a 12-week yoga program during pilot training. If the program proves effective, the authors hypothesize “that this method will enhance operational performance and, subsequently, elevate flight safety”.

Burnout and stress pose significant threats to aviation safety. In *The mechanisms linking perceived stress to pilots’ safety attitudes*, Yanzeng et al. studied the links between stress, cognitive flexibility, and burnout. Their results demonstrate a significantly negative correlation between pilots’ perceived stress and their safety attitude, highlighting the critical role of cognitive flexibility and the complex impact of job burnout. The COVID-19 pandemic exacerbated these stressors. In *Challenges and support needs in psychological and physical health among pilots: a qualitative study*, Xu et al. reported that during the pandemic, the “health of pilots was not taken seriously.” Their study aimed to clarify these challenges to inform the development of a more scientific and comprehensive health system for civil aviation pilots.

Fatigue and sleep deprivation remain persistent operational risks. In *Comparison of effects of modafinil and caffeine on fatigue-vulnerable and fatigue-resistant aircrew*, Wingelaar-Jagt et al. described the potential benefits of stimulants during periods of sleep deprivation. The study confirmed “different degrees of performance degradation” and suggested that “stimulants might be especially useful for fatigue-vulnerable individuals.” Compounding the issue of fatigue, Shi et al. investigated sleep disorders in Chinese airline pilots. In *Association of age and night flight duration with sleep disorders among Chinese airline pilots*, they reported that aging and monthly night flight duration had a synergistic, negative effect on sleep, calling for urgent exploration and intervention. Finally, addressing trauma is essential for long-term crew health, and, in *Assessment policy of post-traumatic stress disorder in aviation*, Vuorio et al. suggested the global adoption of the International Classification of Diseases (ICD-11) criteria for stress disorders to standardize the assessment and treatment of aircrew.

To support these efforts, accurate screening and diagnostic tools are indispensable. In *Echocardiography screening of German military pilot applicants*, Guettler and Sammito analyzed 14.5 years of echocardiograms to determine how often cardiac diseases were diagnosed and influenced aeromedical decision-making, providing valuable data for screening protocols in high-hazard occupations. Similarly, understanding occupational risks is crucial. In *Prevalence and risk factors of occupational neck pain in Chinese male fighter pilots*, Yang et al. pointed to the need for “appropriate training schedules and a more holistic perspective on musculoskeletal

protection” to mitigate a common ailment among fighter pilots. Even environments on Earth can offer insights. In *Short-term changes in chest CT images among individuals at low altitude after entering high-altitude environments*, Wang P. et al. reported on pathologies such as spontaneous mediastinal emphysema that occur during high-altitude adaptation, offering a terrestrial analog for understanding physiological stress.

This Research Topic of studies adds crucial links for safeguarding human capital in the rapidly evolving aerospace sector. The combined insights into physiological countermeasures, mental resilience, and occupational health create a clear, evidence-based agenda. This work supports the ongoing need to manage risk and enhance performance, ensuring that the next great leaps in aviation and space exploration are both ambitious and safe.

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Association of age and night flight duration with sleep disorders among Chinese airline pilots

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Objective: Night flights might aggravate sleep disorders among aging airline pilots, posing a threat to flight safety. In this study, we assess the prevalence of sleep disorders as well as the combined effects of night flight duration and aging on sleep disorders.

Method: A cross-sectional study was conducted between July and December, 2021. Participants were recruited from a commercial airline. Sleep disorders were evaluated using the Pittsburgh Sleep Quality Index (PSQI). The interaction effect of night flight duration and age on sleep disorders and their correlates were examined using logistic regression models.

Results: In total, 1,208 male airline pilots were included in the study, with a median age of 34 (interquartile range [IQR]: 29–39) years. The overall prevalence of sleep disorders was 42.6%. The multivariate logistic regression identified an interaction between night flight duration and age on sleep disorders (adjusted odds ratio [aOR] of the interaction term was 5.85 95% CI: 2.23–15.34 for age \geq 45 years; 1.96 95% CI: 1.01–3.81 for the age group 30–44 years). Longer night flight duration (aOR: 4.55; 95% CI: 1.82–11.38) and body mass index (BMI) \geq 28.0 kg/m² (aOR: 0.16; 95% CI: 0.03–0.91) were significantly associated with sleep disorders in participants aged \geq 45 years. Hyperuricemia (aOR: 1.54; 95% CI: 1.09–2.16) and regular exercise (aOR: 0.23; 95% CI: 0.08–0.70) were significantly associated with sleep disorders in the 30–44 years age group.

Conclusion: The mean monthly night flight duration and aging had a synergistic effect on airline pilots' sleep disorders, implying an aging and work-related mechanistic pathogenesis of sleep disorders in airline pilots that requires additional exploration and intervention.

KEYWORDS

age, night flight duration, interaction, sleep disorders, PSQI

1. Introduction

Previous studies have shown that sleep disorders increase the risk of adverse health outcomes, including obesity, diabetes, cardiovascular diseases, and neurodegenerative diseases (1). Sleep disorders are also responsible for mental health issues such as anxiety, depression, and suicidal ideation (2, 3) and are significantly associated with increased risk of death and accidents (4). Notably, sleep disorders in pilots are a major concern for flight safety. Sleep reduction can

make an impact on behavioral alertness and cognitive performance (5), which may reduce pilots' alertness during flight, resulting in a decline in attention, memory, reaction ability, and driving ability, and even causing flight accidents in severe cases.

Studies conducted on airline pilots have shown a similarly high prevalence of sleep disorders. In a cross-sectional study involving 328 Gulf Cooperation Council commercial airline pilots, 34.1% of participants experienced excessive daytime sleepiness, and 45.1% of individuals reported falling asleep at the controls at least once without first consenting to sleep with their coworkers (6). Another study using the Pittsburgh Sleep Quality Index (PSQI) to measure general sleep quality showed that 38.5% of airline pilots had sleep disorders (7). However, this study was of small sample size, comprising only 41 participants. Most recently, research including 749 aircrew members, 74.1% of whom were pilots, discovered that 45.9% of aircrew members had at least one sleep problem, 24.6% of participants had already involuntarily fallen asleep on board while on duty, and 15.5% of aircrew members had excessive daytime sleepiness (8). However, this study was performed during the COVID-19 pandemic, with many airline pilots not flying at usual times, which might not reflect the impact of flight duty on sleep.

Age was found to be one of the most important factors in predicting sleep health. A previous polysomnographic study of in-flight sleep showed that older aircrew members had longer sleep latencies, more awakenings and arousals, and a smaller number of sleep periods, indicating the impact of age on the quantity and quality of sleep (9). Furthermore, shift work, physical stress at work, current disease, hectic schedules, and gender all contribute to the development of sleep disorders among the general population (10). For airline pilots, their shifting arrangement, demanding work schedules, and time zone changes cause circadian desynchronization and finally lead to the occurrence of sleep problems (11–13). For example, constant stimulation of artificial light and maintaining alertness during the night flight duty may influence circadian clockwork and make them subject to difficulty falling asleep and insomnia after they finish flight duty. However, the question remains as to how night flight duty might impact sleep health. Of note, changes in circadian properties are also associated with aging (14). The molecular circadian clockwork is intricately linked to a number of aging-related signaling pathways (15). As night flight duty itself would disturb the circadian machinery, causing sleep disorders further, it might accelerate sleep disorders among aging airline pilots who are prone to sleep problems. However, no research has been conducted to study the synergistic (interaction) effects of night flight duration and aging on sleep among airline pilots.

This study was designed to investigate the prevalence of sleep disorders among airline pilots and to determine if there is an interaction between age and flight time and sleep disorders. Age-specific correlates that might contribute to the high prevalence of sleep disorders among airline pilots were also examined.

2. Materials and methods

2.1. Study design and participants

In this cross-sectional study, 1,209 male airline pilots who routinely received a standardized comprehensive physical

examination were enrolled from the Shanghai Hospital of Civil Aviation Administration of China, Gubei Branch of Ruijin Hospital Affiliated with the School of Medicine, Shanghai Jiaotong University from July to December, 2021. One participant was excluded for missing data on age, night flight duration, and sleep disorder variables, leaving 1,208 airline pilots with validated information for the final analysis.

The study was approved by the Institutional Review Board (IRB) of Shanghai Hospital of the Civil Aviation Administration of China (Yi Ke Lun Shen No.11[2020]). All participants gave informed consent before taking part in this study.

2.2. Assessment of sleep disorders

Sleep disorders were obtained by using PSQI, an instrument that measured the pattern and subjective quality of sleep among airline pilots (7). In general, this 19-item scale measures seven main dimensions of sleep, including subjective sleep quality, sleep efficiency, sleep duration, sleep latency, daytime dysfunction, use of sleep medications, and sleep disturbances. These dimensions of healthy sleep were used to generate a global sleep quality score, ranging from 0 to 21. A higher score indicated poorer sleep quality, and a cut-off value of >5 for the global score denoted poor sleep quality in this study (16).

2.3. Data collection

All participants completed a standardized structured questionnaire to evaluate demographics (age, education level, and marital status), lifestyle (smoking status, alcohol use, and exercise), work-related characteristics (flight duration and flight duty in recent year), and physical examination. Smoking status was classified as “never,” “previous,” or “current” according to self-reported information, and regular alcohol use was defined as a self-reported frequency of alcohol use of more than once a week. Regular exercise was defined as engaging in exercise more than three times per week.

The mean monthly flight duration in the 3 years from 2018 to 2020 was obtained by questionnaire and reported by airline pilots themselves. Night flight duration was defined as the length of time of flying a plane between 30 min before sunset to 30 min after sunrise. A long-haul flight was defined as a flight lasting more than 6 h and crossing six time zones. The mean monthly night flight duration and mean monthly long-haul flight duration were both divided into two groups: <30 vs. ≥30 h per month. Similarly, the mean monthly total flight duration was also measured and divided into two groups: <60 h per month versus ≥60 h per month. The flight duty was categorized as student pilot, co-pilot, captain, and pilot instructor.

Height and weight were measured in light clothing by trained public health workers and were used to calculate the body mass index (BMI), the result of body weight divided by height squared (kg/m^2). According to the criteria of the Working Group on Obesity in China criteria (17), BMI was divided into three groups: normal ($<24.0 \text{ kg}/\text{m}^2$), overweight ($24.0 - <28.0 \text{ kg}/\text{m}^2$), and obese ($\geq 28.0 \text{ kg}/\text{m}^2$). The data on uric acid (UA) was extracted from the hospital's electronic

medical records system, and hyperuricemia (HUA) was defined as $UA \geq 420 \mu\text{mol/L}$ (18).

2.4. Statistical analysis

Continuous variables were expressed as median (interquartile range, IQR) and categorical variables as numbers and percentages. For continuous variables, the t-test or Wilcoxon Scores test was used, and for categorical variables, the Chi-square test or Fisher's exact test was used, as appropriate. To assess the linear trend effect of age on sleep disorders, linear models were employed, with age groups treated as the continuous variable. Logistic regression analysis was performed to investigate the interaction between age and mean monthly night flight duration on sleep disorders, including additive and multiplicative effects, and indicators such as relative excess risk due to interaction (RERI) were used accordingly. Univariate and multivariate logistic regression models were used to calculate the odds ratios (ORs) with 95% confidence intervals (CIs) of mean monthly night flight duration for sleep disorders stratified by age.

We also conducted a sensitivity analysis to investigate the interactive effect of age and mean monthly night flight duration on sleep disorders using a different PSQI global score cutoff value, where a cutoff value of >8 was defined as poor sleep quality in this sensitive analysis. All statistical analysis was performed using Stata 15.0 (Stata Corporation, College Station, TX, USA). A p -value of <0.05 indicated statistical significance (two-sided).

3. Results

3.1. Participant characteristics

Characteristics of aviation pilots with sleep disorders are presented in Table 1. A total of 1,208 participants were included in this study, with a median age of 34 (IQR: 29–39) years. All participants were men, and 573 (47.4%) had a mean monthly night flight duration of ≥ 30 h in previous three years. Participants with sleep disorders were likely to be in group of 30–44 years, show a lack of physical activity, and have more current smoking, HUA, a longer monthly flight time, and a longer night flight time (p s < 0.05).

3.2. Prevalence of sleep disorders

Overall, 515 (42.6%) participants were detected to have sleep disorders using the PSQI scale. The prevalence of sleep disorders was significantly higher in airline pilots who had night flight durations of ≥ 30 h than in airline pilots who had a mean monthly night flight duration of < 30 h in previous 3 years (43.5 vs. 36.5%, $p = 0.014$). However, inconsistent results were observed across age groups. In the age group ≥ 45 years, individuals with a longer mean monthly night flight had a significantly higher prevalence of sleep disorders (≥ 30 h: 48.9 vs. < 30 h: 23.1%, $p = 0.001$). However, in the < 30 years age group, no significant difference was observed in the prevalence of sleep disorders between different

night flight groups (< 30 h: 35.0% vs. ≥ 30 h: 28.1%, $p = 0.236$). Similarly, in the group aged 30–44 years, the prevalence of sleep disorders was 40.2% among airline pilots with night flight durations of < 30 h, compared with 45.6% among those who had night flight durations of ≥ 30 h ($p = 0.138$; Figure 1). Moreover, the prevalence of sleep disorders that increased with age was only observed in individuals with night flight durations of ≥ 30 h in previous 3 years when stratified by night flight duration ($p_{\text{trend}} = 0.005$).

3.3. Joint associations of age and mean monthly night flight time with sleep disorders

Given the disparity in the prevalence of sleep disorders among different ages by night flight time, we performed the multivariate logistic regression analysis to examine the joint associations of age and mean monthly night flight time on sleep disorders adjusted for education, marital status, smoking status, regular alcohol use, regular exercise, BMI, HUA, flight duty, mean monthly flight duration in previous 3 years, and mean monthly long voyage duration in previous 3 years (Table 2).

In multivariate logistic regression models including the interaction between age and night flight duration on sleep disorders, the adjusted odds ratio (aOR) of interaction term between age and night flight duration on the multiplicative scale was 5.85 (95% CI: 2.23–15.34, $p < 0.001$), and the measure of effect modification on the additive scale of RERI was 2.00 (95% CI: 0.63–3.36, $p = 0.004$), but only for the ≥ 45 years age group. For the moderately older age group (30–44 years), the hypothesis of the additive interacted effect between mean monthly night flight duration and moderate older age on sleep disorders should be rejected ($p = 0.433$); while the aOR of interaction terms on the multiplicative scale were 1.96 (95% CI: 1.01–3.81, $p = 0.047$), suggesting that the hypothesis of multiplicative effect between age and night flight duration on sleep disorders was accepted. These results show an aggravating effect of night flight duration on sleep health as the age of airline pilots increases (Table 2).

3.4. Age-specific correlates of sleep disorders

Table 3 presents the results of multivariate logistic regression analysis stratified by age groups. The result indicates that longer night flight duration (aOR = 4.55, 95% CI: 1.82–11.38, $p = 0.001$) and BMI of $\geq 28.0 \text{ kg/m}^2$ (aOR = 0.16, 95% CI: 0.03–0.91, $p = 0.039$) were significantly associated with sleep disorders in the ≥ 45 years age group. Among the 30–44 years age group, sleep disorders were positively associated with HUA (aOR = 1.54, 95% CI: 1.09–2.16, $p = 0.013$) but negatively associated with regular exercise (aOR = 0.23, 1 95% CI: 0.08–0.70, $p = 0.010$).

3.5. Sensitive analysis

In sensitive analysis, the interaction term of age and mean monthly night flight duration on sleep disorders lost its statistical significance using the PSQI global score ≥ 8 as a cutoff value for sleep disorders. However, in a multivariate logistic regression model

TABLE 1 Characteristics of aviation pilot by sleep disorders.

Variables	Total (n = 1,208)	Sleep disorders		p-value
		No (n = 693)	Yes (n = 515)	
Age groups, yrs				0.009
<30	323 (26.7)	216 (29.7)	107 (22.2)	
30–44	726 (60.1)	413 (56.8)	313 (65.1)	
45–62	159 (13.2)	98 (13.4)	61 (12.7)	
Median (IQR)	34(29–39)	34(29–39)	34(30–38)	0.410
Education				0.721
Technical degree	47 (3.9)	28 (3.9)	19 (3.9)	
Bachelor's degree	1,136 (94.0)	682 (93.8)	454 (94.4)	
Master's degree	25 (2.1)	17 (2.3)	8 (1.7)	
Marital status				0.064
Single	898 (74.4)	523 (71.9)	375 (78.0)	
Currently married	263 (21.7)	173 (23.8)	90 (18.7)	
Other	47 (3.9)	31 (4.3)	16 (3.3)	
Smoking				0.015
Current	351(29.1)	188 (26.0)	162 (33.6)	
Never	667(55.2)	417 (57.4)	251 (52.1)	
Previous	190(15.7)	121 (16.6)	69 (14.3)	
Alcohol use	77(6.4)	39 (5.4)	38 (7.9)	0.077
Regular exercise	50(4.1)	38 (5.2)	12 (2.5)	0.020
BMI, kg/m ²				0.859
<24.0	511(44.2)	309 (44.4)	202 (43.7)	
24.0 – <28.0	529(45.6)	314 (45.1)	215 (46.5)	
≥28.0	118(10.2)	73 (10.5)	45 (9.8)	
HUA	417(34.5)	228 (31.4)	189 (39.3)	0.005
Flight duty in the previous year				0.494
Student pilot	91(7.5)	59 (8.1)	32 (6.6)	
Co-pilot	565(46.8)	329 (45.3)	237 (49.2)	
Captain	261(21.6)	157 (21.6)	104 (21.6)	
Pilot instructor	291(24.1)	182 (25.0)	109 (22.6)	
Mean monthly total flight duration >60 h in previous 3 years	1,020(84.4)	600 (82.5)	420 (87.3)	0.025
Mean monthly long-haul duration >30 h in previous 3 years	643(53.2)	373 (51.3)	270 (56.0)	0.100
Mean monthly night flight duration >30 h in previous 3 years	573 (47.4)	324 (44.6)	249 (51.7)	0.014

IQR, interquartile range; BMI, body mass index; HUA, hyperuricemia. Texts in bold type indicate statistical significance.

without interaction terms, mean monthly night flight duration was significantly associated with sleep disorders (aOR = 2.12, 95% CI: 1.35–3.33). In an age-specific regression model, the mean monthly night flight duration was significant in the 30–44 years age group (aOR = 2.19, 95% CI: 1.27–3.78) and the ≥45 years age group (aOR = 5.63, 95% CI: 1.06–29.94; [Supplementary Table S1](#)).

4. Discussion

In this cross-sectional study comprising 1,208 male airline pilots, we found a relatively high prevalence of sleep disorders among airline

pilots. We identified a positive association of age and night flight duration with sleep disorders in airline pilots. Specifically, the mean monthly night flight duration of ≥30 h in previous 3 years was significantly associated with a higher risk of sleep disorders in pilots aged ≥45 years. Moreover, age-specific factors including clinical and lifestyle characteristics were also observed. To our knowledge, this is the largest study exploring the prevalence of sleep disorders by PSQI scale and the association of age and night flight duration with it among airline pilots in Asia.

Sleep problems are common in shift workers, such as healthcare professionals (39.2%) (19), night shift autoworkers (56.2%) (20), and firefighters (59.3%) (21), and their prevalence is relatively higher

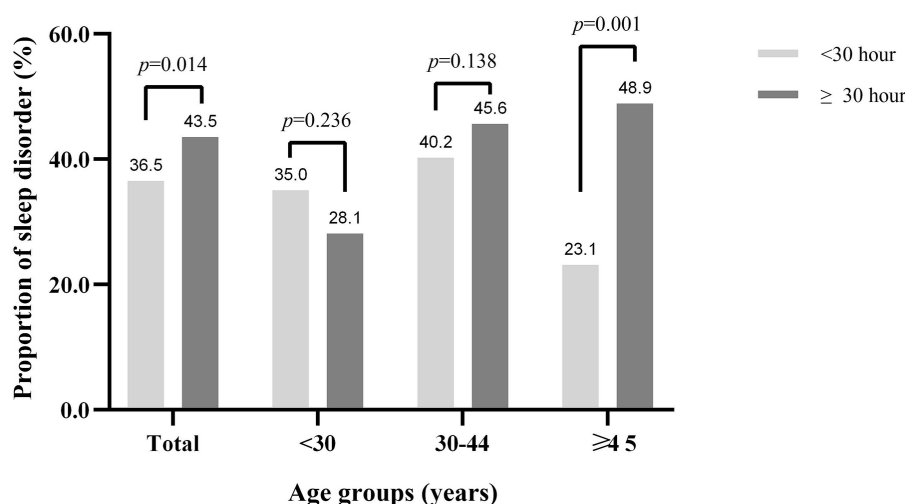


FIGURE 1

The proportion of sleep disorders by age groups and mean monthly night flight duration in previous 3 years. Test for trend by age for sleep disorders was significant only in the group with night flight durations of ≥ 30 h in previous 3 years ($p_{\text{trend}} = 0.005$).

TABLE 2 Joint associations of age and mean monthly night flight duration with sleep disorders.

Age groups	<30 h		≥ 30 h		aOR (95% CI); p for >30 vs. <30 within strata of age group	Measure of effect modification on additive scale: RERI (95% CI)	Measure of effect modification on multiplicative scale: point estimate (95% CI)
	N with/without outcome	aOR (95% CI)	N with/without outcome	aOR (95% CI)			
<30	85/234	1.00	29/89	0.63 (0.34–1.15) $p = 0.134$	0.63 (0.33–1.22) $p = 0.173$	Reference	Reference
30–44	139/336	1.42(0.88–2.29) $p = 0.150$	192/390	1.75 (1.07–2.86) $p = 0.026$	1.17(0.83–1.64) $p = 0.373$	0.70(–1.05–2.46) $p = 0.433$	1.96 (1.01–3.81) $p = 0.047$
45–62	24/65	0.61(0.26–1.42) $p = 0.250$	49/94	2.23 (1.07–4.65) $p = 0.032$	4.88(1.97–12.11) $p = 0.001$	2.00(0.63–3.36) $p = 0.004$	5.85 (2.23–15.34) $p < 0.001$

RERI, relative excess risk due to interaction. aOR, adjusted odds ratio; aORs are adjusted for education, marital status, smoking status, regular alcohol use, regular exercise, BMI, hyperuricemia, flight duty, mean monthly flight duration in previous 3 years, and mean monthly long voyage duration in previous 3 years. Texts in bold type indicate statistical significance.

than the general population (16.6–35.9%) (22–24). In this study, we observed a higher prevalence of sleep disorders in professional airline pilots, mirroring the result obtained from national commercial pilots in Saudi Arabia (6, 7). Sleep problems are one of the problems concerning airline pilots since lack of good sleep causes fatigue and decrements in performance and consequently poses a threat to flight safety. Previous studies used wrist-based actigraphy to measure or estimate individuals' sleep amounts during flight duty, based on which rest schemes were made to solve sleep problems, but some findings countered the current literature and recommendations (25, 26). Therefore, more large population-based studies were needed to provide evidence of sleep and fatigue management.

It has been hypothesized that age-related changes in the human circadian pacemaker and sleep homeostatic mechanisms play a pivotal role in the hallmarks of age-related changes in sleep (27). Both subjective and objective measures of sleep indicate that sleep patterns and characteristics change with increasing age, and the prevalence of sleep disorders is higher among older adults (28, 29). In this study,

we found an increasing prevalence of sleep disorders by age, in agreement with previous studies.

Although the flying duration and flight duty times of each pilot are restricted and proper rest periods are mandated by China Civil Aviation Regulations to guarantee flight safety, sleep disorders remain a common problem among airline pilots. In this study, only the mean monthly night flight duration was significantly associated with sleep disorders. Notably, our results show an interactive effect of mean monthly night flight duration and age on sleep, which suggests that duration of night flight and age are not isolated factors for sleep disorders. Among airline pilots aged ≥ 45 years, longer night flight duration increases the risk of sleep disorders, which suggests a complex impact of aging on circadian rhythms. Although how aging affects the circadian clock is still unclear, aging could weaken the circadian clock, disrupt sleep–wake cycles, reduce the ability of peripheral organs to coordinate circadian rhythms, and change the circadian clock output at the molecular level (15). The long night flight time could cause more sleep problems in senior pilots since night flights have been linked to circadian rhythm disturbance. The findings

TABLE 3 Factors associated with sleep disorders by age groups.

Variables	Aged <30 years		Aged 30–44 years		Aged ≥45 years	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Age, year	1.04(0.87–1.24)	0.652	0.98(0.93–1.04)	0.547	1.04(0.95–1.14)	0.405
Education						
Technical degree	1.00		1.00		1.00	
Bachelor's degree	-	-	-	-	1.09(0.42–2.82)	0.857
Master's degree	2.60(0.15–44.38)	0.509	0.86(0.29–2.53)	0.780	0.31(0.03–3.28)	0.330
Marital status						
Single	1.00		1.00		1.00	
Currently married	0.78(0.44–1.41)	0.412	0.77(0.43–1.36)	0.366	-	-
Others	0.97(0.08–12.21)	0.980	0.59(0.29–1.20)	0.145	0.61(0.10–3.73)	0.596
Smoking						
Current	1.00		1.00		1.00	
Never	0.65(0.36–1.17)	0.153	0.79(0.55–1.12)	0.181	1.35(0.52–3.50)	0.541
Previous	0.46(0.16–1.30)	0.142	0.65(0.40–1.06)	0.085	1.28(0.50–3.26)	0.604
Alcohol use in previous 3 years	2.36(0.45–12.26)	0.307	1.22(0.66–2.28)	0.522	1.21(0.36–4.09)	0.764
Regular exercise	1.84(0.47–7.14)	0.378	0.23(0.08–0.70)	0.010	0.34(0.08–1.42)	0.139
BMI, kg/m ²						
<24.0	1.00		1.00		1.00	
24.0 – <28.0	0.90(0.53–1.54)	0.706	0.99(0.70–1.38)	0.937	0.61(0.28–1.30)	0.199
≥28.0	0.79(0.32–1.95)	0.607	0.83(0.49–1.40)	0.475	0.16(0.03–0.91)	0.039
HUA	1.27(0.75–2.14)	0.372	1.54(1.09–2.16)	0.013	1.94(0.87–4.34)	0.106
Flight duty in the previous year						
Student pilot	1.00		1.00		1.00	
Co-pilot	0.81(0.42–1.57)	0.533	0.86(0.11–6.81)	0.884	-	-
Captain	-	-	0.66(0.08–5.46)	0.703	-	-
Pilot instructor	-	-	0.61(0.07–5.08)	0.645	1.07(0.47–2.45)	0.871
Mean monthly total flight duration >60 h in previous 3 years	1.78(0.93–3.40)	0.080	1.02(0.50–2.10)	0.952	1.07(0.25–4.57)	0.925
Mean monthly long-haul duration >30 h in previous 3 years	0.56(0.29–1.09)	0.086	1.20(0.83–1.72)	0.332	0.70(0.25–1.95)	0.497
Mean monthly night flight duration >30 h in previous 3 years	0.63(0.33–1.22)	0.173	1.17(0.83–1.64)	0.369	4.55(1.82–11.38)	0.001

BMI, body mass index; HUA, hyperuricemia. Texts in bold type indicate statistical significance.

in our study indicate the necessity for age-specific night flight time restrictions among airline pilots.

Consistent with other findings that short night sleep duration is associated with a higher risk of HUA (30), our data also shows a positive relationship between HUA and sleep disorders, but only among airline pilots aged 30–44 years. Moreover, we could not determine whether high levels of UA lead to sleep disorders in this study. In this study, we observed that regular exercise was negatively associated with sleep disorders among middle-aged and older adult airline pilots, although the association was not significant for those aged ≥45 years, which suggests that regular exercise habits might benefit sleep. In contrast to a previous study, which showed a negative association between obesity and sleep health (31), we found that obesity was positively associated with

sleep health among airline pilots aged over 45 years, which needs further investigation. It has been reported that men's sleep is more prone to be influenced by aging than women's (32). However, limited by the gender of the participants, we are unable to explore this.

Sleep disturbance not only contributes to biological aging, cognitive aging, and depression (33) but is also associated with cardiovascular disease and related harmful outcomes (34, 35). A meta-analysis, which comprised 61 original studies from 71 different populations, has revealed a significant negative effect of sleep restriction on cognitive processing across cognitive domains (36). Moreover, sleep disturbances are associated with faster chronic disease accumulation, which points towards the importance of early detection and treatment of sleep disturbances in older adults (37).

Our findings reveal the necessity of sleep management as a possible strategy to reduce chronic multimorbidity and guarantee flight safety for airline pilots. An age-specific arrangement of restricted duty time and scientific rest, which would be helpful to pilots' health and extend their careers, would be beneficial for commercial airline companies in the long term.

This study has several limitations. First, we conducted a cross-sectional study; therefore, we could not confirm the causation between the development of sleep disorders and associated factors of interest, such as HUA and regular exercise. Nevertheless, it was unlikely to influence our finding of the synergistic effect of age and mean monthly night flight time on sleep disorders. Second, sleep disorders were determined by self-reported questionnaires but not polysomnography. Self-report data are prone to information bias, as participants might exaggerate or understate their sleep problems. However, as participants completed the questionnaire individually without any intervention from their colleagues or healthcare workers, the results pooled from the questionnaires should reflect the real sleep problems of airline pilots at the population level. Moreover, a standard PSG is usually conducted in a sleep lab with a certified sleep technician present throughout the study, which is time-consuming and complex for a population-based epidemiological study. A recent study suggested that subjective sleep quality was significantly associated with changes in cortisol levels that reflect the circadian rhythm of the Hypothalamic–Pituitary–Adrenal (HPA) axis (38). Therefore, the PSQI would be a proper measure of pilots' sleep issues, especially in large-scale population studies. Third, all participants were recruited from one commercial airline company, which may limit the generalizability of the results in view of different airline arrangements and rest schemes in airline companies. However, we only examine the association of mean monthly night flight duration with sleep disorders in this study. Therefore, our observed association should not be affected. Finally, the results may not generalize to female airline pilots because they are limited to male pilots.

5. Conclusion

We found that the mean monthly night flight time and aging had a synergistic effect on airline pilots' sleep disorders, with those who were ≥ 45 years old and had longer night flight durations being at higher risk. We also discovered that the overall prevalence of sleep disorders increased with age. However, no such occurrence was observed among those whose average monthly night flying duration was < 30 h, emphasizing the importance of proper night flight duty assignment in consideration of age. Extra consideration should be given to the negative effects of metabolic changes on sleep disorders. Additionally, regular exercise may help middle-aged airline pilots sleep better.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary material](#), further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Institutional Review Board (IRB) of Shanghai Hospital of the Civil Aviation Administration of China. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

RS contributed to the data analysis and interpretation and drafted the manuscript. LF and FW contributed to the conception and design of the work and data collection. LF and WX critically reviewed the manuscript. LF generally supervised the study. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpubh.2023.1217005/full#supplementary-material>

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Prevalence and risk factors of occupational neck pain in Chinese male fighter pilots: a cross-sectional study based on questionnaire and cervical sagittal alignment

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Background: Neck pain (NP) is a common musculoskeletal disorder among fighter pilots and has become a rising concern due to its detrimental impact on military combat effectiveness. The occurrence of NP is influenced by a variety of factors, but less attention has been paid to the association of NP with demographic, occupational, and cervical sagittal characteristics in this group. This study aimed to investigate the prevalence and risk factors of NP in Chinese male fighter pilots using a questionnaire and cervical sagittal measurements.

Methods: Demographic and flight-related data, as well as musculoskeletal pain information, were gathered from Chinese male fighter pilots via a self-report questionnaire. Cervical sagittal parameters were measured and subtypes were classified using standardized lateral cervical radiographs. Differences in various factors between the case and control groups were analyzed using t-tests or chi-square tests. Binary logistic regressions were conducted to explore potential risk factors contributing to NP. Predictors were presented as crude odds ratios (CORs) and adjusted odds ratios (AORs), along with their respective 95% confidence intervals (CIs).

Results: A total of 185 male fighter pilots were included in this cross-sectional study. Among them, 96 (51.9%) reported experiencing NP within the previous 12 months. The multivariate regression analysis revealed that continuous flight training (AOR: 4.695, 95% CI: 2.226–9.901, $p < 0.001$), shoulder pain (AOR: 11.891, 95% CI: 4.671–30.268, $p < 0.001$), and low back pain (AOR: 3.452, 95% CI: 1.600–7.446, $p = 0.002$) were significantly associated with NP.

Conclusion: The high 12-month prevalence of NP among Chinese male fighter pilots confirms the existence of this growing problem. Continuous flight training, shoulder pain, and low back pain have significant negative effects on pilots' neck health. Effective strategies are necessary to establish appropriate training schedules to reduce NP, and a more holistic perspective on musculoskeletal protection is needed. Given that spinal integrated balance and compensatory

mechanisms may maintain individuals in a subclinical state, predicting the incidence of NP in fighter pilots based solely on sagittal characteristics in the cervical region may be inadequate.

KEYWORDS

neck pain, neck injury, sagittal balance, spinal curvatures, military pilots, risk factors, injury prevention, injury assessment

1. Introduction

Non-combat injuries are the leading cause of pilot attrition and military discharge in modern warfare (1). Spine-related pain, such as neck pain (NP) and its association with occupational hazards, is a well-documented complaint among military pilots (2). Unlike helicopter or transport aircraft pilots, fighter pilots usually experience high G-forces, repetitive head and neck flexion and rotation, and added weight from the helmet and oxygen equipment (3–5), which increase the load on the cervical vertebrae, especially during neck rotation and extension (6, 7). These specific occupational factors place fighter pilots at a higher risk of spinal injury presenting as NP than helicopter and transport pilots (8), not to mention the general population (9).

The prevalence of NP in fighter pilots has increased significantly due to the ever-increasing intensity of flight training (10, 11), with reports of up to 83% in a 12-month period and up to 97% over the course of a career (3). While some cases of ligamentous disruption, vertebral fractures, and disk pathologies that require surgery have been documented (12, 13), most fighter pilots self-report mild to moderate non-specific NP (14, 15). However, such NP is often reported to have a negative impact on a pilot's physical and mental health (16), manifesting as impaired attention and concentration, poor motor control, postural instability, inability to perform in-flight maneuvers, task interruption, and temporary or permanent grounding (13, 17). These harmful impacts on individual health and operational capability can lead to substantial losses in military interests (12), especially through attrition and early career termination (17). It is noteworthy to consider that training an operational military pilot costs around \$9 million (12), and even higher at \$15.2 million for a single fighter pilot (17). Therefore, effective and efficient preventive measures are needed to reduce the high incidence of NP among military pilots. Combined with appropriate medical management, this may enable military pilots to avoid suffering long-term pain and disability, thus ensuring good military strength. However, before developing and recommending preventive strategies and keeping medical readiness, injury assessment models must first identify prevalence rates and etiological factors (17, 18).

Cervical sagittal alignment and balance play a crucial role in maintaining physiological function of the cervical spine and serve as critical indicators in evaluating cervical degeneration. These include sagittal curvature, sagittal displacement, and various cervicothoracic junction parameters (19–22). Previous research has shown differences in cervical sagittal parameters, specifically cervical lordosis (C2–C7 angle) (15), T1 slope (19, 23, 24), and C2–7 sagittal vertical axis (SVA) (19, 24), between healthy individuals and patients with NP. Additionally, pain is prevalent in other regions of the body, such

as the shoulder and lower back (25), which may worsen the impact of NP. In addition, age, inappropriate BMI, and smoking habit may be associated with a higher risk of developing NP (26, 27). These predictive factors may resemble those found in previous research on NP in the general population, but no study has comprehensively investigated the factors associated with the occurrence of NP in the population of fighter pilots with regard to the above areas. At present, research on occupational factors has primarily focused on flying time or experience, such as total, annual, or weekly flying hours (4, 15, 17, 28–33) and duration of occupational exposures (31, 34, 35). However, there has been neglect in investigating the impact of flight training schedules on NP, such as continuous or non-continuous flight training. The purpose of this cross-sectional study was to assess the prevalence of occupational NP in Chinese fighter pilots and to determine associated factors by analyzing demographic and occupational information and cervical sagittal characteristics.

2. Methods

2.1. Study design and participants

This cross-sectional study was designed to investigate the prevalence and associated risks of NP in Chinese male fighter pilots using a questionnaire survey and radiological measurements. The Ethics Committee of the Air Force Medical Center of the People's Liberation Army of China (PLA) approved the study (No. 2023-11-PJ01) and it was conducted in accordance with the Helsinki Declaration. Before the study commenced, written informed consent was obtained from all participants. The participants were recruited at the Air Force Medical Center using independently controlled quota sampling based on military theater command distribution, and data collection began from August 2021 to November 2022. The survey was anonymous and self-administered, with a paper copy of the questionnaire distributed to each enrolled participant. The X-ray examinations were performed by the Radiology Department of the Air Force Medical Center of the PLA.

All male participants were actively serving in Air Force military units in the Five Theater Commands of the PLA. They were certified fighter pilots aged between 20 and 48. The exclusion criteria for the participants were as follows: (1) any current or past history of known trauma or surgery to the spine and joints, signs of neurological deficit, or structural lesions; (2) under medical treatment for physical pain; (3) systemic disease affecting the musculoskeletal system (e.g., osteoarthritis, rheumatoid arthritis, etc.); and (4) absence from flying for more than four consecutive weeks in the previous 12 months (e.g., vacation, study, etc.). A formula for estimating prevalence study was

employed to determine the sample size for this study. An expected NP prevalence of 51% (10) and a margin of error of 15% were considered, resulting in a required sample size of 172. To account for potential power loss due to invalid responses or radiographs, an additional 15% was added, bringing the final number of invited pilots to 198. A total of 198 male pilots participated in the study, with 41 serving in the Eastern Theater Command, 40 in the Southern Theater Command, 39 in the Western Theater Command, 41 in the Northern Theater Command, and 37 in the Central Theater Command. However, only 185 participants were ultimately enrolled, with 37 in the Eastern Theater Command, 38 in the Southern Theater Command, 36 in the Western Theater Command, 38 in the Northern Theater Command, and 36 in the Central Theater Command. The dropout data were: (1) six pilots completed invalid questionnaires due to missing items; (2) seven pilots took non-standard radiographs with questionable anatomical locations or unclear image markings.

2.2. Questionnaire measures

The complete list of items in the questionnaire can be found in [Appendix](#). The study's questionnaire comprised three sections as follows:

Section 1: Baseline characteristics of the participants such as age, height, weight, and smoking status. Weight of the participants was measured to the nearest 0.1 kg using a digital scale while wearing light clothing. Standing height was measured to the nearest 0.5 cm. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, to the nearest 0.1 kg/m². Current smokers were defined as having smoked at least 100 cigarettes in their lifetime and having smoked in the past 30 days, with two response options (yes/no).

Section 2: This section was based on records of aircraft piloting. The occupational data included total flying hours (flying hours in a career) and annual flying hours (flying hours in the past 12 months). As total or annual flying time may only provide an ambiguous description of cumulative chronic exposure within a career or 12 months, we defined an indicator reflecting flight training schedules: continuous flight training refers to ≥ 6 h per week (1) for more than 4 consecutive weeks in the past 12 months, with two response options (yes/no). Service units were surveyed to confirm the practicability of quota sampling according to military theater distribution. However, this data were not used as a variable in the study due to limited access to display military details.

Section 3: This section utilized a modified version of the validated Nordic Musculoskeletal Questionnaire (1, 36) to evaluate the prevalence of musculoskeletal symptoms (pain). The body parts, including neck, shoulders, upper back, elbows, lower back, wrists/hands, hips/thighs, knees, and ankles/feet, were defined by shaded areas on body maps ([Appendix](#)). Three questions were developed for each body part, including: (1) "In your career, have you had any pain, discomfort, or numbness in this area?" (yes/no); (2) "In the past 12 months, have you had any pain, discomfort, or numbness in this area?" (yes/no); and (3) "In the past 12 months, have you been prevented from doing normal activities (e.g., work, housework, hobbies) because of this condition?" (yes/no).

A preliminary questionnaire was utilized in a prior investigation (1). To ensure that the questions were relevant and comprehensible, a

board of specialists in clinical medicine, epidemiology, and aeromedicine content validated the questionnaire. Before the formal study, this pre-questionnaire was piloted with 20 people to test the language and logical order of each question, and to slightly modify the question with unclear meaning and specify the completion requirements as the final form. A question about alcohol abuse was removed because it was deemed unsuitable and unreliable for this profession. In order to obtain more statistically valid, homogeneous, and generalizable results, pilots were asked to complete baseline data (Section 1) that would be aligned with their electronic medical records at the time of enrollment (10). Additionally, to enhance reliability of flying experience and to minimize recall bias, participants were asked to report data on occupational characteristics (Section 2) according to their flight logs (10). Flight logs were completed by the pilot based on mission status, reviewed by the unit commander and flight surgeon, and provided to the medical provider at the time of the medical evaluation. In this study, NP was defined as any reported pain, discomfort, or numbness in the past 12 months that interfered with work, housework, or hobbies (37). The participants were informed of their rights and assured their privacy would be protected to minimize reporting bias. The data collection was conducted in closed rooms to ensure privacy and limit outside influences. Trained investigators were assigned to explain the questionnaire at the distribution site. The 12-month prevalence of NP was calculated as the percentage of all participants who answered "yes" to both questions (1–3) about the neck in Section 3. For statistical analysis, pilots were categorized into NP group (reporting any NP in the previous year) and non-NP group (not reporting any NP in the previous year) according to the NP presentation identified by the questions.

2.3. Radiographic measures

All radiographs were taken under identical conditions using the same procedure as described below. The participants stood upright and gazed straight ahead while keeping their shoulders fully relaxed and their arms naturally hanging at their sides. The cervical spine films were taken at a source-subject distance (SSD) of 150 cm with the beam centered at C4, approximately at the level of the mandibular angle (38). All subjects were positioned and imaged by the same researcher, an 8-year veteran radiologic technologist. The Luminos DRF Max (Siemens Healthcare GmbH, Erlangen, Germany) was used as the radiographic machine. The radiographs were recorded on an Imaging Clinical Information System (ICIS; version 2014.1.SU6.5, AGFA HealthCare N.V., Mortsel, Belgium) at a resolution of 1,928 × 2,308 pixels.

Cervical sagittal parameters were calculated for each participant, as displayed in [Figure 1](#). The definition of each measured parameter (39–45) was listed in [Table 1](#). According to the description outlined above, three experienced spine surgeons, blinded to subject grouping, independently measured all the sagittal parameters of 185 radiographs using Surgimap software (version 2.3.2.1, Nemaris, New York, NY, United States) (43). The results of these measurements were averaged to present the final data for this study. The measurements were also subject to evaluation of inter-rater reliabilities using intraclass correlation coefficients (ICCs) and average measures. The standard interpretations of the ICCs were as follows: 0.00–0.50 (poor reliability), 0.50–0.75 (moderate reliability), 0.75–0.90 (good reliability),

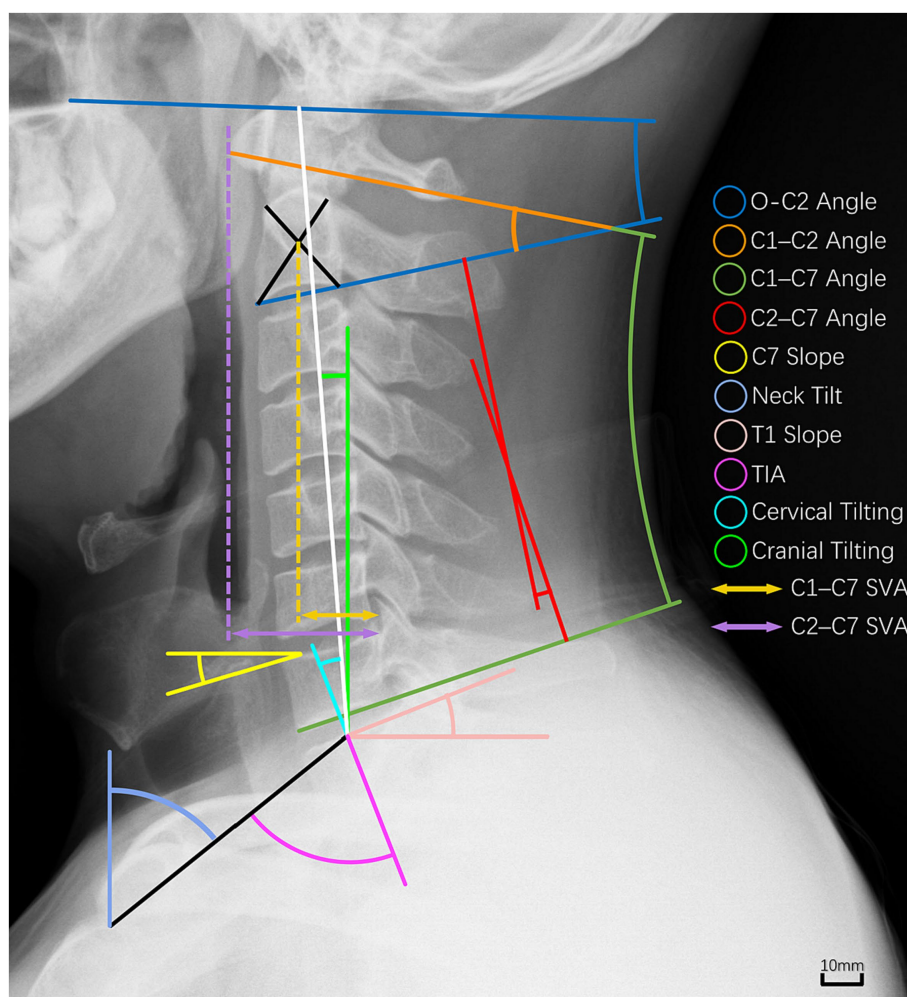


FIGURE 1
Measured cervical sagittal parameters of the study in the lateral cervical radiograph.

and >0.90 (excellent reliability) (46). Excellent reliability was observed for the parameters measured with O-C2 angle ($ICC=0.992$, $p < 0.001$), C1-C2 angle ($ICC=0.980$, $p < 0.001$), C1-C7 angle ($ICC=0.984$, $p < 0.001$), C1-C7 SVA ($ICC=0.997$, $p < 0.001$), C2-C7 angle ($ICC=0.995$, $p < 0.001$), C2-C7 SVA ($ICC=0.996$, $p < 0.001$), neck tilt ($ICC=0.958$, $p < 0.001$), TIA ($ICC=0.958$, $p < 0.001$), T1 slope ($ICC=0.973$, $p < 0.001$), cervical tilting ($ICC=0.983$, $p < 0.001$), cranial tilting ($ICC=0.942$, $p < 0.001$), and T1S-CL ($ICC=0.983$, $p < 0.001$). Good reliability was reported for the C7 slope ($ICC=0.889$, $p < 0.001$).

Cervical sagittal alignment classifications were evaluated using a modified method of Toyama et al. (47). The contour tangents to the four sides of the C3-C6 vertebral bodies were constructed by connecting adjacent corners with a straight line. Each pair of diagonally opposite corners where adjacent contour tangents intersected was connected by a line, respectively, (Figure 2). The intersection of these two lines is the vertebral centroid. Line AB was constructed to connect midpoint A on the inferior surface of C2 and midpoint B on the superior surface of C7. The alignment was then classified as lordotic, straight, sigmoid, or kyphotic based on the relative positions of the centroids to the line AB (Figure 2). The cervical sagittal alignment of

the 185 radiographs was independently classified into lordotic, straight, sigmoid, or kyphotic groups by the same three orthopedic surgeons using Surgimap software as described above. The final subtype for each participant was determined by majority rule. Inter-rater agreement among the classifications was evaluated using the Fleiss kappa coefficient. The kappa values were categorized as follows: 0.00–0.20 (slight agreement), 0.21–0.40 (fair agreement), 0.41–0.60 (moderate agreement), 0.61–0.80 (substantial agreement), and 0.81–1.00 (almost perfect agreement) (48). In this study, the inter-rater agreement for the classifications demonstrated almost perfect agreement with a Fleiss kappa coefficient of 0.889 ($p < 0.001$).

2.4. Statistical analysis

Statistical analyses were conducted using SPSS software (version 26.0, Chicago, United States). The questionnaire and radiographic measurement results were presented as mean \pm standard deviation for quantitative data and as absolute values with percentages for qualitative data. Data normality was assessed using the Kolmogorov–Smirnov test (1). Differences in normally distributed quantitative data between the

TABLE 1 Definition of cervical sagittal parameters which were used in this study.

Parameter	Definition
O-C2 angle	The angle between McGregor's line (the line connecting posterior edge of the hard palate to the opisthion) and the lower endplate of C2.
C1-C2 angle	The angle between the line connecting the inferior anterior arch and the inferior posterior arch of C1 and the inferior endplate of C2.
C1-C7 angle	The angle between the line connecting the inferior anterior arch and the inferior posterior arch of C1 and the inferior endplate of C7.
C1-C7 SVA	The distance from the posterosuperior corner of C7 and the perpendicular to the center of the anterior edge of the C1 body.
C2-7 angle	The angle between the C2 lower endplate and the C7 lower endplate. The C2-7 angle is also referred to as C2-7 lordosis (CL).
C2-7 SVA	The distance from the posterosuperior corner of C7 and the perpendicular to the center of the C2 body.
C7 slope	The angle between a horizontal line and the upper endplate of C7.
T1 slope (T1S)	The angle between a horizontal line and the superior endplate of T1 on a standing lateral radiograph (T1S = cervical tilting + cranial tilting).
Neck tilt (NT)	The angle between the line connecting the center of the T1 upper endplate and the top of the sternum and the vertical line extending from the sternum tip.
Thoracic inlet angle (TIA)	The angle between the line connecting the center of the T1 superior endplate and the top of the sternum and the vertical line extending from the center of the T1 superior endplate (TIA = T1S + NT).
Cervical tilting	The angle between the line through and perpendicular to the center of the T1 upper plate and the line from the center of the T1 upper plate to the tip of the dens.
Cranial tilting	The angle between the line from the center of the T1 upper endplate to the dens and the perpendicular through the center of the T1 upper endplate.
T1S-CL	The T1S minus the C2-7 lordosis (CL).

O-C2, Occiput-C2; SVA, Sagittal vertical axis; and CL, C2-7 lordosis.

NP and non-NP groups were assessed using independent two-sample *t*-tests. Cohen's *d* values were calculated using G*Power software to evaluate significant effects (49). The Cohen's *d* values were categorized as follows: 0.00–0.10 (negligible effect), 0.10–0.20 (small effect), 0.20–0.50 (medium effect), 0.50–0.80 (large effect), and >0.80 (very large effect) (50). Differences in non-normally distributed quantitative or qualitative data between the NP and non-NP groups were assessed using chi-square tests with two-tailed Cramer's *V* coefficient. The Cramer's *V* values were categorized as follows: 0.00–0.10 (small association), 0.10–0.30 (medium associations), 0.30–0.50 (large association), and >0.50 (very large association) (51). For multiple comparisons of NP prevalence among cervical sagittal subtypes, chi-square tests were conducted followed by Bonferroni analyses (50). Univariate and multivariate logistic regression analyses were performed to identify variables influencing the prevalence of NP in fighter pilots. All possible variables were included in the multivariate logistic regression, and a stepwise elimination procedure was applied to control for potential confounders to determine the simplest and most accurate regression model. Crude odds ratios (CORs) and adjusted odds ratios (AORs) along with their corresponding 95% confidence intervals (CIs) were reported. The model fit was assessed using Hosmer-Lemeshow goodness of fit test. The Hosmer-Lemeshow statistic indicates a poor fit if the significance value is less than 0.05 (50). All *p* values were two-tailed, and *p* < 0.05 was considered statistically significant.

3. Results

3.1. Demographic and occupational characteristics of the participants and pain prevalence

Table 2 shows the background data of the study participants. A total of 185 male fighter pilots were included in this study, with a mean age of 28.5 ± 6.0 years, mean height of 173.8 ± 3.6 cm, mean body

weight of 70.8 ± 7.1 kg, mean BMI of 23.4 ± 2.1 kg/m², mean total flying time of 996.5 ± 835.6 h, and mean annual flying time of 151.9 ± 34.3 h. Almost half of the pilots reported continuous flight training in the past year (57.3%), while the other half did not (42.7%). Current smoking was reported by 70 (37.8%) pilots, and 116 (62.7%) had a BMI of less than 24 kg/m².

Among 185 participants, 96 (51.9%) reported NP (95% CI: 44.6–59.2%), 72 (38.9%) reported low back pain (95% CI: 31.8–46.0%), and 59 (31.9%) reported shoulder pain (95% CI: 25.1–38.7%) in the past 12 months (Table 2).

As demonstrated in Table 2, the incidence of NP was significantly higher in pilots with continuous flight training than in pilots without continuous flight training (68.9 vs. 29.1%, *p* < 0.001, Cramer's *V* = 0.394, *p* < 0.001); however, the NP and non-NP groups did not differ significantly in total flying hours (*p* = 0.449) and annual flying hours (*p* = 0.069). In addition, significant differences were found in the incidence of NP according to pain in other areas of the body. The incidence of NP was 88.1% in the patients with shoulder pain (*p* < 0.001, Cramer's *V* = 0.496, *p* < 0.001) and 66.7% in the patients with low back pain (*p* = 0.001, Cramer's *V* = 0.236, *p* < 0.001). There were no significant differences in age, height, weight, BMI, or smoking history between the NP and non-NP groups.

3.2. Cervical sagittal characteristics of the participants

The cervical sagittal characteristics of the subjects, including parameters and alignment subtypes, are shown in Table 3. The distribution of cervical sagittal alignment subtypes in the total cohort was as follows: lordotic subtype in 61 (33.0%), straight subtype in 80 (43.2%), sigmoid subtype in 20 (10.9%), and kyphotic subtype in 24 (13.0%). In other words, the lordotic subtype accounted for 33.0% of the total cohort compared to 67.0% for the non-lordotic subtype.

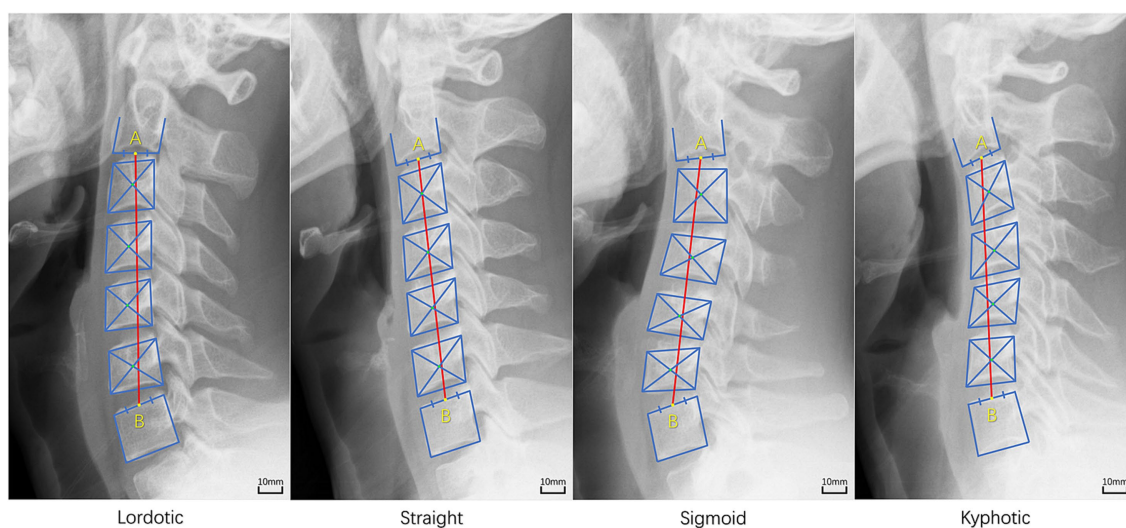


FIGURE 2

The method of subtype classification of cervical sagittal alignment [modified method of Toyama et al. (47)]. Lordotic: all centroids (green colored dot) are anterior to the line AB (red colored line) and the distance between at least one centroid and the line AB is 2 mm or more; Straight: the distance between the line AB and each centroid is less than 2 mm; Sigmoid: some centroids are anterior and some are posterior to the line AB and the distance between the line AB and at least one centroid is 2 mm or more; Kyphotic: all centroids are posterior to the line AB and the distance between at least one centroid and the line AB is 2 mm or more.

As shown in Table 3, no significant differences were found between participants with and without NP in O-C2 angle, C1-C2 angle, C1-C7 angle, C1-C7 SVA, C2-C7 angle, C2-C7 SVA, C7 slope, neck tilt, TIA, T1 slope, T1S-CL, cervical tilting, or cranial tilting. Multiple comparisons analysis revealed that there were no significant differences in the incidences of NP according to cervical sagittal subtypes ($p = 0.81$, Cramer's $V = 0.074$, $p = 0.81$). The incidence of NP was 47.5% in the lordotic group, 53.8% in the straight group, 50.0% in the sigmoid group, and 58.3% in the kyphotic group.

3.3. Risk factors associated with NP

Unadjusted and adjusted analyses using logistic regression were performed to assess risk factors associated with NP among the study participants (Table 4). Multivariate regression analysis revealed that continuous flight training, shoulder pain, and low back pain were significantly predictive of NP. However, the following factors were not significantly associated with the incidence of NP: age, height, weight, BMI, smoking, total flying time, annual flying time, cervical sagittal parameters, and subtypes. Participants with continuous flight training were 4.695 times more likely to have NP than those without continuous flight training (AOR: 4.695, 95% CI: 2.226–9.901, $p < 0.001$). In addition, shoulder pain (AOR: 11.891, 95% CI: 4.671–30.268, $p < 0.001$) and low back pain (AOR: 3.452, 95% CI: 1.600–7.446, $p = 0.002$) were associated with the incidence of NP.

4. Discussion

4.1. Main findings

The aim of this study was to determine the incidence of occupational NP among fighter pilots in the Chinese Air Force and to

evaluate potential risk factors by analyzing demographic and occupational data as well as cervical sagittal measurements. The main finding of the study was that NP in pilots was positively associated with continuous flight training, shoulder pain, and low back pain, but there was no evidence of an association between measured cervical sagittal parameters and subtypes and NP. These results could provide supportive evidence for maintaining spinal health and preventing injury in military pilots.

4.2. Epidemiology of NP in fighter pilots

In this cross-sectional study, a high prevalence of musculoskeletal conditions was found, with 51.9% of respondents reporting prominent NP compared to a mean prevalence of 37% in the general population aged 17–70 years (9). Consistent with some studies, NP prevalence in fighter pilots ranged from 47 to 83% (3, 7, 15, 30, 52, 53). In contrast, lower prevalence of NP was reported in other studies (1, 4, 54, 55). The variations in prevalence observed across studies may be attributed to discrepancies in the target populations, time intervals considered, or criteria used to characterize pain and associated symptoms (15, 17). For example, differences in the time frames used to define NP are evident. A study by Vanderbeek et al. (56) found that the 3-month prevalence of NP (51%) was lower than the 12-month prevalence (64%) in fighter pilots. This discrepancy may be attributable to the shorter time frame used to define NP, which may have decreased recall bias. Another illustration is whether or not medical treatment was sought. Yang et al. (1) reported that NP necessitating medical care had a 3-month prevalence rate of 30%, whereas Ang et al. (57) did not take into account seeking care, which had a 3-month prevalence rate of 53%. It should be noted that certain military pilots may hesitate to report experiencing pain and seek medical assistance due to concerns over flight restrictions (10). This could potentially affect the described prevalence of self-reported pain. Consequently, the lack of

TABLE 2 Background data for all participants and for NP and non-NP groups.

	Total (<i>N</i> = 185)	NP group (<i>N</i> = 96)	Non-NP group (<i>N</i> = 89)	Cohen's <i>d</i> or Cramer's <i>V</i>	<i>p</i> value
Demographic data					
Age (year)	28.5 ± 6.0	28.8 ± 5.6	28.1 ± 6.4	0.124	0.400 ^a
Height (cm)	173.8 ± 3.6	173.9 ± 3.8	173.7 ± 3.4	0.043	0.772 ^a
Weight (kg)	70.8 ± 7.1	71.3 ± 7.4	70.3 ± 6.7	0.137	0.352 ^a
BMI (kg/m²)	23.4 ± 2.1	23.5 ± 2.1	23.3 ± 2.0	0.127	0.389 ^a
< 24 kg/m² (<i>n</i>)	116 (62.7%)	59 (50.9%)	57 (49.1%)		
≥ 24 kg/m² (<i>n</i>)	69 (37.3%)	37 (53.6%)	32 (46.4%)		
Current smoking					
Yes (<i>n</i>)	70 (37.8%)	42 (60.0%)	28 (40.0%)	0.127	0.085 ^b
No (<i>n</i>)	115 (62.2%)	54 (47.0%)	61 (53.0%)		
Occupational data					
Total flying hours (h)	996.5 ± 835.6	1041.4 ± 821.5	948.1 ± 852.6	0.112	0.449 ^a
Annual flying hours (h)	151.9 ± 34.3	156.3 ± 35.5	147.2 ± 32.6	0.269	0.069 ^a
< 150h (<i>n</i>)	88 (47.6%)	44 (50.0%)	44 (50.0%)		
≥ 150h (<i>n</i>)	97 (52.4%)	52 (53.6%)	45 (46.4%)		
Continuous flight training					
Yes (<i>n</i>)	106 (57.3%)	73 (68.9%)	33 (31.1%)	0.394	<0.001 ^b
No (<i>n</i>)	79 (42.7%)	23 (29.1%)	56 (70.9%)		
Pain in other body areas					
Shoulder pain					
Yes (<i>n</i>)	59 (31.9%)	52 (88.1%)	7 (11.9%)	0.496	<0.001 ^b
No (<i>n</i>)	126 (68.1%)	44 (34.9%)	82 (65.1%)		
Low back pain					
Yes (<i>n</i>)	72 (38.9)	48 (66.7)	24 (33.3)	0.236	0.001 ^b
No (<i>n</i>)	113 (61.1)	48 (42.5)	65 (57.5)		

^aIndependent two-sample *t*-test was used; ^bChi-square test was used.

standardized definitions has been identified as a limitation in these studies.

The gaps could be addressed through Delphi studies, which are likely to establish uniform definitions of both NP and neck regions to improve the accuracy of future results (10). We suggest identifying specific population characteristics, such as age, gender, aircraft type, flight experience, and any other relevant demographic or occupational variables, as a first step. Then, it is recommended to define NP using recognized diagnostic criteria or standardized measurement tools that are commonly used in evaluating NP. The Dutch Musculoskeletal Questionnaire, Neck Disability Index (NDI), or Visual Analog Scale (VAS) are examples of such tools that can effectively identify the anatomical location, severity, frequency, and duration of pain. Body maps with shaded areas or self-reported markings can be used to indicate the specific regions of discomfort. Consider implementing a severity grading system and establishing a timeframe for NP to capture variations in severity and frequency of symptoms. It is worth noting that whether the definition should include criteria for functional impairment or limitations in performing specific tasks related to flight duties should be determined. Additionally, it is necessary to evaluate the extent to which the injury or pain requires medical assistance. Thirdly, one should ensure that the defined criteria

are validated and consistent with established clinical or research standards. It is also crucial that the definition is effectively communicated to researchers, healthcare providers, and other stakeholders involved in the study or management of NP in this population.

4.3. Do demographic characteristics affect the incidence of NP in fighter pilots?

As people age, their risk of developing NP in the general population might increase due to inadequate body mass index (BMI) and smoking habits (26, 27). However, the relationship between demographic factors and NP in fighter pilots remains inconclusive, likely due to the impact of occupational and physical functional characteristics, as well as social-psychological factors such as a high volume of flight missions, prolonged computer or desk work (28, 54), reduced neck strength or torque (7), and mental fatigue or anger (54).

Some recent studies have shown that age is a risk factor for NP in fighter pilots (4, 28). However, our study found no significant association between age and NP, which is consistent with other reports (7, 31, 54). While increasing age is a non-modifiable risk factor for NP

TABLE 3 Cervical sagittal characteristics for all participants and for NP and non-NP groups.

	Total (N = 185)	NP group (N = 96)	Non-NP group (N = 89)	Cohen's d or Cramer's V	p value
Cervical sagittal parameter					
O-C2 angle (deg)	15.1 ± 6.6	15.6 ± 6.4	14.5 ± 6.7	0.163	0.269 ^a
C1-C2 angle (deg)	24.5 ± 5.8	24.8 ± 5.9	24.1 ± 5.7	0.133	0.369 ^a
C1-C7 angle (deg)	28.8 ± 9.1	29.0 ± 9.9	28.5 ± 8.3	0.061	0.681 ^a
C1-C7 SVA (mm)	33.7 ± 10.7	33.4 ± 11.1	34.1 ± 10.4	0.069	0.641 ^a
C2-C7 angle (deg)	5.1 ± 9.5	5.1 ± 9.8	5.1 ± 9.2	0.002	0.987 ^a
C2-C7 SVA (mm)	18.6 ± 8.6	18.3 ± 8.9	18.9 ± 8.4	0.070	0.636 ^a
C7 slope (deg)	17.5 ± 6.6	17.2 ± 5.2	17.8 ± 7.8	0.087	0.554 ^a
Neck tilt (deg)	46.3 ± 6.1	46.1 ± 5.4	46.5 ± 6.8	0.059	0.692 ^a
TIA (deg)	67.8 ± 7.5	67.7 ± 6.7	68.0 ± 8.4	0.041	0.780 ^a
T1 slope (deg)	21.5 ± 5.4	21.5 ± 5.2	21.5 ± 5.2	0.009	0.953 ^a
T1S-CL (deg)	16.4 ± 7.7	16.4 ± 7.8	16.3 ± 7.7	0.004	0.978 ^a
Cervical tilting (deg)	18.5 ± 5.9	18.7 ± 6.3	18.3 ± 5.4	0.067	0.648 ^a
Cranial tilting (deg)	3.0 ± 4.3	2.8 ± 4.3	3.3 ± 4.3	0.113	0.442 ^a
Cervical sagittal subtype					
Lordotic subtype (n)	61 (33.0%)	29 (47.5%)	32 (52.5%)	0.074	0.801 ^b
Straight subtype (n)	80 (43.2%)	43 (53.8%)	37 (46.2%)		
Sigmoid subtype (n)	20 (10.8%)	10 (50.0%)	10 (50.0%)		
Kyphotic subtype (n)	24 (13.0%)	14 (58.3%)	10 (41.7%)		

^aIndependent two-sample *t*-test was used; ^bChi-square test was used. Deg, degree; mm, millimeter.

in general occupational groups (58), numerous individual-related and flight-specific factors could be confounded by age for military pilots. For example, young pilots, such as trainees, typically fly low to medium performance aircraft, such as the K-8 and J-7. These pilots do not exhibit any pathological changes in the spine due to low cumulative load exposures. However, they have limited flight experience, lack awareness of effective pre- and in-flight precautions, such as warming up with range of motion and isometrics and placing their head against the seat, and are not sufficiently trained for G-load resistance. Pilots between the ages of 30 and 40 demonstrate optimal flight skills, possess knowledge of preventative measures for neck injuries, and maintain excellent physical fitness. However, many of these pilots operate high-performance fighter aircraft, such as the J-16 and J-20, which impose high peak loads during numerous flight missions. As a result, the cumulative loads have caused gradual degeneration of the spine. For pilots over 40 years old, flight training volume is reduced gradually. Flight skills and preventive measures remain mature, and rest and recovery time is longer. However, the physical function has deteriorated, making it difficult to withstand the burden of flight loads on the body, with degenerative spinal disease appearing gradually. Thus, in this study, the association between age and NP may be attenuated by the interaction of both positive and negative factors associated with the age factor.

Neck pain is generally not directly caused by smoking. However, smoking may indirectly contribute to certain factors such as reduced blood flow, impaired healing, degenerative disk disease, coughing and breathing problems, and lifestyle factors that may increase the risk of NP (59). Unlike age, smoking is a modifiable factor that can be reduced or stopped (58). Our study discovered a greater occurrence of smoking

within the NP group compared to the non-NP group. However, this difference was not significant, and several previous studies also failed to discover a significant association between smoking and NP (17, 54). We assessed smoking through a yes/no question concerning the past 30-day and lifetime tobacco usage, a crude measure of this form of exposure. By classifying individuals who formerly smoked as non-smokers and those who smoke only a few cigarettes per month or day as smokers, the exposure characterization may be imprecise. This possible crude classification of exposure is likely non-differential, potentially weakening the associations.

Consistent with previous studies (32, 33), our study did not find a significant association between NP and BMI. While BMI is a measure of body fat based on an individual's weight and height, it is not directly related to NP, nor does it take into account the distribution of body fat. Individuals with higher muscle mass may have a greater BMI without excess body fat. Conversely, someone with a lower BMI may still have a larger percentage of body fat concentrated in specific regions, such as the neck. Fat accumulation around the neck may be linked to NP, but BMI alone does not determine its occurrence. Future studies on NP in this population should consider incorporating additional anthropometric measures such as body fat percentage, fat distribution, and muscle mass. It is worth noting that the average BMI of pilots in our sample was below 24, which may imply lower muscle mass in younger pilots. This may be due to loosely supervised physical training programs, as well as frequent deployments and relocations that prevent pilots from having regular access to the gym for training and make it difficult to obtain counterbalanced training equipment.

The present study did not demonstrate a significant relationship between height and NP, in contrast to the findings of a previous study

TABLE 4 Logistic regression analysis of risk factors potentially associated with NP.

Variables	Univariate analysis		Multivariate analysis	
	COR (95% CI)	<i>p</i> value	AOR (95% CI)	<i>p</i> value
Demographic data				
Age (years)	1.021 (0.973–1.072)	0.398		
Height (cm)	1.012 (0.935–1.096)	0.770		
Weight (kg)	1.020 (0.979–1.063)	0.351		
BMI (kg/m ²)	1.064 (0.925–1.223)	0.388		
Current smoking (Yes vs. No)	1.694 (0.928–3.095)	0.086		
Occupational data				
Total flying hours (h)	1.000 (1.000–1.000)	0.447		
Annual flying hours (h)	1.008 (0.999–1.017)	0.072		
Continuous flight training (Yes vs. No)	5.386 (2.851–10.175)	<0.001	4.695 (2.226–9.901)	<0.001
Pain in other body areas				
Shoulder pain (Yes vs. No)	13.844 (5.800–33.043)	<0.001	11.891 (4.671–30.268)	<0.001
Low back pain (Yes vs. No)	2.708 (1.463–5.014)	0.002	3.452 (1.600–7.446)	0.002
Cervical sagittal parameter				
O-C2 angle (deg)	1.025 (0.981–1.072)	0.268		
C1-C2 angle (deg)	1.023 (0.973–1.076)	0.367		
C1-C7 angle (deg)	1.007 (0.975–1.039)	0.679		
C1-C7 SVA (mm)	0.994 (0.967–1.021)	0.639		
C2-C7 angle (deg)	1.000 (0.970–1.031)	0.987		
C2-C7 SVA (mm)	0.992 (0.959–1.026)	0.634		
C7 slope (deg)	0.987 (0.943–1.032)	0.554		
Neck tilt (deg)	0.990 (0.945–1.038)	0.688		
T1A (deg)	0.994 (0.957–1.033)	0.777		
T1 slope (deg)	1.002 (0.950–1.057)	0.953		
T1S-CL (deg)	1.001 (0.964–1.039)	0.978		
Cervical tilting (deg)	1.012 (0.963–1.063)	0.646		
Cranial tilting (deg)	0.974 (0.910–1.042)	0.440		
Cervical sagittal subtype				
Straight subtype (vs. Lordotic subtype)	1.282 (0.658–2.500)	0.465		
Sigmoid subtype (vs. Lordotic subtype)	1.103 (0.402–3.031)	0.849		
Kyphotic subtype (vs. Lordotic subtype)	1.545 (0.595–4.012)	0.372		

COR, Crude odds ratio; AOR, Adjusted odds ratio; CI, Confidence interval.

(28). Ergonomically, the impact of height on NP appears to be twofold, as both extremely tall and short individuals are at higher risk. Shorter individuals may need to lift their arms more extensively, while taller individuals may need to lean their head forward more often, underlining the importance of appropriate height in confined cockpits. Nevertheless, as aircraft and equipment ergonomics continue to improve, it appears that this effect is decreasing.

4.4. Do fighter pilots with shoulder pain and low back pain have an increased risk of NP?

In the present study, shoulder pain and low back pain were discovered to be independent risk factors for NP in fighter pilots. This

outcome suggests a relationship between shoulder pain, low back pain, and NP, potentially associated with flight posture. As pilots sustain a seated position and stable lower body, there is an increased requirement for push-pull movements with the upper extremities (1). The position required to grip the handle with the hands and fingers results in static contraction of the neck and shoulder muscles, which act as stabilizers to maintain the arms at a perpendicular angle (15). Shoulder pain or muscle fatigue may cause the neck muscles, such as the upper trapezius and scalene, to assist in elevating or shrugging the shoulder to stabilize and control the scapula and arms. This compensation principle weakens the arm and shoulder and strains the neck muscles excessively, leading to pain. It appears to apply to the lumbar region as well. Muscles that act on the spine, including erector spinae and multifidus, may tire from continuous or repeated exposure

to high G-forces, prolonged static postures or both. This could alter the sitting posture by increasing the kyphosis in the lumbar region and potentially changing the regular curvature in the proximal spine area (34). To maintain trunk balance and a forward gaze, the pilot may need to compensate by further extending the neck. This scenario could leave the pilot more susceptible to neck and lower back injuries and pain. Therefore, it is clear that the musculoskeletal system should be analyzed holistically. We should pay close attention to the possibility of NP in individuals who are suffering from shoulder or low back pain. Physical exercise, particularly comprehensive training that incorporates both endurance and strength, should be prioritized as it has been proven to have significant protective effects against NP (52, 60). Ergonomic adjustments to aircraft and flight equipment could potentially affect these compensatory effects, which result from interactions between distinct regional muscles. Therefore, such considerations must be incorporated into new aircraft and equipment designs.

4.5. Is NP related to flying time and training schedules?

On one hand, the total number of flying hours can partially indicate the duration of being in a particular occupational environment. Pilots' neck muscles are significantly activated during flight, suggesting that the neck muscles are subjected to high loads (61). Although exposure to high G-forces may initially strengthen the neck (62), it is widely acknowledged that long-term exposure to such high load pressures contributes to acute or chronic episodes of NP (1, 8, 35, 63). If these loads persist over a period of time, the muscles may tire, thus potentially increasing the risk of neck muscle strain injury (13). Meanwhile, the total time spent in flight can serve as an indicator of flight experience, which to some extent may demonstrate the pilot's flight skills or proficiency. The total flying time is an essential reference index for classifying Air Force ranks, ranging from flying cadets to top pilots. Pilots who have accumulated more flying hours are expected to possess greater flying experience or skill. Previous studies have shown a higher incidence of NP in pilots with lengthy total flying hours (4, 28, 29). However, our investigation concluded that there was no significant association between total flying hours and NP among fighter pilots. This outcome was similar to those of other published studies (30–33). The absence of significant association may be attributed to the interaction of positive and negative factors related to total flying hours, similar to the factor of age. Pilots with comparatively lower total flight time could also encounter NP if they consistently encounter high G-forces during their flights. Meanwhile, pilots who have accumulated significant flight time may not experience frequent and severe NP declines to the same degree if they have taken measures to skillfully avoid the adverse effects of high G-forces, or if they have spent more time in a state of relatively low load level flight.

Pilots who operate the same type of aircraft may encounter varying factors due to the complexity of military missions and changing flight schedules (1). Therefore, annual flying time is inadequate evidence as it only provides an imprecise description of cumulative chronic exposure within a rough time frame instead of flight training distribution. This is evident in the lack of a significant association between annual flying time and NP in our study.

Flight-related NP usually appears acutely during or after flight training and takes several days to recover (16). Flying for more than 6 h per week for four consecutive weeks results in prolonged exposure to G-forces in a relatively short time and inadequate recovery time (1), which may increase the risk of NP in fighter pilots. Our findings support this perspective, demonstrating that fighter pilots who receive continuous flight training have a 4.695 times higher risk of developing occupational NP than pilots who do not receive such training. Following this risk assessment, efforts should be directed toward creating preventive measures. Intermittent flight training or distributing the training volume could potentially mitigate the incidence of NP. For instance, if the yearly training volume stays the same, flight instruction could be completed in 1 week, followed by a week of rehabilitative and physical conditioning training, alternating between the two. This organized scheduling, supervised management, and evaluation of the impacts of these interventions for NP warrant additional research in the future.

Overall, there may be some correlation between flight time data and NP for fighter pilots, but it is not the sole or primary determining factor. Other factors, such as G-forces, dynamic movements, cockpit ergonomics, physical conditioning, and individual variations, also play significant roles in the development of NP. Proper ergonomic design, rigorous pilot training, consistent exercise, and attentive posture within the cockpit can reduce the risk of NP in fighter pilots, irrespective of their total, annual, or weekly flying time (17). Furthermore, upcoming research studies must aim to identify more precise determinants of NP in this group, like exposure to high G-forces per unit time.

4.6. Can cervical sagittal characteristics predict NP in fighter pilots?

This study showed no significant differences in cervical sagittal parameters between individuals with and without NP. This finding aligns with previous research that found no link between NP and cervical spine curvature changes (23, 64–69). One possible explanation for the lack of differences may be that cervical sagittal parameters are not connected to NP. However, some studies have reported contradictory results. A cross-sectional study performed by Jouibari et al. (19) discovered that the NP group, among individuals with cervical lordosis, had a lower C2-7 SVA and T1 slope angle as compared to the healthy control group. This could be a compensatory action to bring the center of gravity of the head back to the spinal axis by reducing T1 slope and C2-7 SVA. However, this phenomenon varies significantly in patients with cervical kyphosis. Li et al. (24) found that the compensation mechanism of the posterior neck muscles facilitates the maintenance of cervical sagittal balance when accompanied with a lower T1 slope and smaller C2-7 SVA. Conversely, a larger C2-7 SVA with a higher T1 slope leads to a cervical malalignment that cannot be fully compensated and eventually causes NP. Therefore, a possible reason for not observing discrepancies is that the values of the cervical sagittal parameters might vary, depending on the type of cervical alignment and its associated compensation mechanism (70). Consequently, these dissimilarities cannot be detected in an unclassified sample. In addition, cervical sagittal parameter changes involve a complex compensatory mechanism that may be affected by both cervical spine degeneration and the alignment

of the entire spine, including thoracic kyphosis, lumbar lordosis, and sacral slope (71–73). Thus, the compensatory site of sagittal balance in NP patients might primarily occur in the thoracic, lumbar, or pelvic segments rather than the cervical segment.

In our study, the modified method of Toyama et al. (47) was used to classify cervical sagittal alignment into four subtypes. It was found that approximately half of the individuals in each subtype did not experience NP or were subclinical in the previous 12 months, which is in accordance with several previous studies (74, 75). Although these studies utilized different classification methods, the findings suggest that NP symptoms were only slightly more common in non-lordotic subtypes than in lordotic subtypes, and that the type of cervical kyphosis was not a significant risk factor for NP (24). However, a study by Moon et al. (15) found a significant association between cervical alignment and NP in pilots. Pilots with cervical kyphosis had a significantly higher incidence of NP (81.8%) compared to those with lordosis (41.7%) or straight cervical spine (50%). These inconsistent findings suggest that the conventional view of the “normal” lordotic cervical spine (76) may not be universally applicable and that the natural sagittal alignment of the cervical spine may be morphologically diverse. An alternative viewpoint maintains that cervical misalignments always represent a pathological condition, and the lack of symptoms may indicate that the relationship between misalignment and symptoms has not yet had sufficient time to manifest. For instance, a kyphotic cervical spine increases the likelihood of developing NP due to the extra load on the neck muscles that support the weight of the head (77, 78). The compensatory response to increased load is based on excessive muscle contraction and increased tension in the small joints of the spine and intervertebral disks. This mechanism can further accelerate the progression of spinal degeneration, leading to a series of related clinical symptoms including NP, low back pain, and shoulder pain (79).

Spinal balance goes beyond the fixed morphological alignment of vertebrae in momentary imaging, and it should be regarded as a synergistic somatic balance of the nervous, muscular, and skeletal systems. We suggest that future studies on NP measure not only traditional static radiographic parameters but also precise dynamic indicators such as neuromuscular coordination, functional tasks, muscle fatigability, muscle size, kinematics, and kinetics. These additional measurements would enable a more thorough assessment of the predictive and interventional implications for NP. It is also important to note that pilots with misaligned cervical spines may still face a higher risk of experiencing more severe and frequent NP under high G-forces, such as during air combat maneuvers, or even cervical spine fractures during ejection, which could lead to paralysis. Thus, early identification of pilots with cervical pathology and special attention to their spinal health is essential. Furthermore, future research should explore the impact of upgraded equipment configurations on the frequency of NP. Implementation of lightweight head-mounted gear, protective anti-G ejection seats, and rocket-powered multi-propulsion systems may considerably enhance prevention and reduce neck injuries in military pilots.

4.7. Limitations

This study provides new insights into occupational NP among Chinese Air Force pilots and advances our comprehension of

musculoskeletal disorders for aeromedical researchers. However, the study has some limitations to be considered. Firstly, our study may be affected by the imprecision of the prior statistical power analysis used to determine the optimal sample size. This is due to the limited research and data available on cervical sagittal characteristics in this military population using cross-sectional methodology. Although the participants came from different Air Force units and were distributed evenly across Chinese military theaters, the generalizability of the findings to the larger population of military pilots may be limited by the inability to identify the entire study population and sample distribution, as well as the relatively small sample size. Therefore, future studies with larger sample sizes and random sampling are needed. Secondly, the cross-sectional nature of the study does not allow for the determination of causality, as there is generally no evidence of the temporal relationship between risk factors and outcomes. Long-term longitudinal studies are necessary to evaluate the root causes of NP in military pilots. Thirdly, this study formed part of a more extensive research initiative, and the implementation of a standardized questionnaire during participant interviews may have resulted in the absence of particular sought-after information, including the frequency, severity, and length of musculoskeletal symptoms. Thus, future research ought to consider these facets along with symptoms originating from other bodily regions, such as hips, knees, and ankles. Additionally, the survey study should be enhanced in the succeeding phase of the intervention study by incorporating information pertaining to physical activity levels, both active and unhealthy lifestyle practices, mobility and flexibility factors, and medical consultation-seeking behavior. Finally, we measured cervical sagittal balance by taking a lateral radiograph of the cervical spine without obtaining global spinal sagittal measurements. Therefore, we were unable to determine the reciprocal influence of other spinal regions, such as the thoracic and lumbar spine. In future studies, we plan to include lateral radiographs of the entire spine to accurately measure the alignment of the spine and determine the relationship between NP and sagittal characteristics.

5. Conclusion

The 12-month prevalence of NP is high among Chinese male fighter pilots. Pilots experiencing low back pain and shoulder pain have a heightened risk of NP. The relationship between shoulder and low back pain and NP warrants further investigation as part of a holistic approach to musculoskeletal injury prevention. Continuous flight training schedules have a significant negative impact on pilots' neck health. Optimizing training schedules to improve rest and prevent fatigue could potentially reduce NP in this occupation. It may be insufficient to predict the incidence of NP in fighter pilots based solely on sagittal characteristics of the cervical spine. Further elaboration of the integrated somatic balance and its compensatory mechanisms may enhance research into the causes of NP.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Ethics Committee of the Air Force Medical Center of the PLA (No. 2023-11-PJ01). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

FY, ZW, HoZ, and BX: methodology, investigation, data curation, formal analysis, visualization, writing-original draft, and writing-review and editing. HuZ, LG, and TeL: methodology, supervision, validation, and writing-review and editing. JZ, ZC, TiL, and XH: investigation, formal analysis, and validation. YC and JD: conceptualization, methodology, project administration, funding acquisition, supervision, and writing-review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpubh.2023.1226930/full#supplementary-material>

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Comparison of effects of modafinil and caffeine on fatigue-vulnerable and fatigue-resistant aircrew after a limited period of sleep deprivation

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Introduction: Literature suggests pilots experience fatigue differently. So-called fatigue-resistant or -vulnerable individuals might also respond differently to countermeasures or stimulants. This study, which is part of a larger randomized controlled clinical trial, aims to investigate the effect of caffeine and modafinil on fatigue-resistant and -vulnerable pilots.

Methods: This study included 32 healthy employees of the Royal Netherlands Air Force, who completed three test days, separated by at least 7 days. After a regular work day, the subjects were randomly administered either 300 mg caffeine, 200 mg modafinil or placebo at midnight. Hereafter the subjects performed the psychomotor vigilance test (PVT), vigilance and tracking test (VigTrack) and Stanford sleepiness scale (SSS) six times until 8 a.m. the next day. Subjects were ranked on the average number of lapses on the PVT during the placebo night and divided into three groups: fatigue-vulnerable (F_{VUL}), -intermediate (F_{INT}) and -resistant (F_{RES}), with 11, 10 and 11 subjects in each group, respectively. Area under the curve (AUC) of the PVT, VigTrack and SSS during the test nights were calculated, which were used in univariate factorial analysis of variance (ANOVA). Tukey's HSD *post hoc* tests were used to differentiate between the groups.

Results: A significant effect of treatment was found in the ANOVA of both PVT parameters, VigTrack mean reaction time and SSS. There was a statistically significant effect of fatigue group on all PVT parameters and VigTrack mean percentage omissions, where F_{INT} and F_{RES} scored better than F_{VUL} . There was a significant interaction effect between treatment and fatigue group for PVT number of lapses. This is congruent for the AUC analyses in which for all parameters (except for the SSS) the performance of the F_{VUL} group was consistently worse than that of the F_{INT} and F_{RES} groups.

Discussion: This study demonstrates that the performance of individuals with different fatigue tolerances are differently affected by stimulants after a limited period of sleep deprivation. The classification of fatigue tolerance through PVT lapses when sleep deprived seems to be able to predict this.

KEYWORDS

aviation, fatigue, shift work, sleep, wakefulness-promoting agents, fatigue tolerance

1 Introduction

With air travel in 2022 increasing to pre-COVID levels, the filing of fatigue reports has increased. In March 2022, Southwest Airline pilots filed 35 reports for every 10,000 duty periods, compared with 10 reports for every 10,000 duty periods in March 2019 (Wallace, 2022). Unfortunately, pilot fatigue not only leads to safety reports, but can and does result in incidents (Wingelaar-Jagt et al., 2021). A recent example is the Ethiopian Airlines pilots who fell asleep during flight and overflowed their destination (Bekele, 2022). Pilots report that the currently high rate of experienced fatigue is most likely due to a shortage of pilots, combined with scheduling difficulties, which are issues that occur worldwide and are difficult to solve (Polek, 2022; Ziemelis, 2023). Even when duty time limitations are adhered to, these issues increase the workload of pilots, one of the contributing factors to fatigue as described by the International Civil Aviation Organization: “A physiological state of reduced mental or physical performance capability resulting from sleep loss, extended wakefulness, circadian phase, and/or workload (mental and/or physical activity) that can impair a person’s alertness and ability to perform safety related operational duties” (International Civil Aviation Organization ICAO, 2020).

However, not all pilots react the same to the fatigue; the level of experienced fatigue and subsequent effect on performance differs highly between individuals (Wingelaar-Jagt et al., 2021). These inter-individual differences in the level of fatigue experienced and the performance decrements are also found in (military) pilots, even in highly trained and selected individuals such as fighter pilots (Petrie et al., 2004; Van Dongen et al., 2006). These differences are robust and stable, i.e., they are most probably individual traits instead of consequences of analyses, sleep history or reactions to the type of sleep loss and therefore difficult to control or change (Van Dongen et al., 2004; Chua et al., 2019; Yamazaki and Goel, 2020). This level of vulnerability has been described as fatigue resistance and fatigue susceptibility, or fatigue-resistant and -susceptible/vulnerable individuals (Harrison et al., 2008).

Recent studies demonstrate that whether individuals are fatigue-resistant or -vulnerable might affect the rate with which stimulants like modafinil influences one’s performance under sleep deprivation (Caldwell et al., 2020; Van Cutsem et al., 2021). Stimulants are used to enhance the performance of fatigued (military) pilots, thereby mitigating the risks associated with fatigue (Institute of Medicine US Committee on Military Nutrition Research, 2001). If the effectiveness of stimulants depends on an individual’s fatigue susceptibility, determining if a pilot is fatigue-resistant or -vulnerable might be useful when advising the pilot whether to take a stimulant.

Unfortunately, distinct characteristics such as sex, race, age, and body mass index are not able to predict whether individuals are

fatigue-resistant or -vulnerable or one’s response to stimulants (Yamazaki and Goel, 2020; Galli et al., 2022). Several methods have been introduced to identify fatigue-vulnerable and -resistant individuals (Yamazaki et al., 2022). A commonly used approach is to look at performance under sleep deprivation and rate individuals with good scores as fatigue-resistant and those with low scores as fatigue-vulnerable (Patanaik et al., 2015; Chua et al., 2019; Caldwell et al., 2020). Another method is to look at the change in performance under sleep deprivation compared with baseline, whereby individuals with little change are considered resilient (Patanaik et al., 2014; Riontino and Cavallero, 2021). A third suggested method is to look at intra-individual variance in performance (Yamazaki et al., 2022). Recent research indicates that all three approaches are comparable for psychomotor vigilance test (PVT) lapses; however, only the first method seems to be effective for subjective sleepiness metrics (Casale et al., 2022; Yamazaki et al., 2022). Predicting fatigue susceptibility by looking at baseline parameters yields promising results, but is not yet perfect (Patanaik et al., 2015; Galli et al., 2022).

This study is part of a larger randomized controlled trial that was designed to investigate several aspects of the implementation of modafinil and caffeine as countermeasures for fatigue in (military) aviation. In a previously published manuscript about this trial, we concluded that both modafinil and caffeine significantly decrease the negative effects of an extended period of continuous wakefulness on vigilance compared with a placebo (Wingelaar-Jagt et al., 2023). The present study compared the effects of modafinil and caffeine administration on the fatigue-vulnerable and -resistant participants of our population. We expected modafinil and caffeine to have a greater effect on the performance of fatigue-vulnerable individuals.

2 Materials and methods

This study is part of a larger randomized controlled trial, for an elaborate description of the materials and methods we therefore also refer to Wingelaar-Jagt et al. (2023) (Wingelaar-Jagt et al., 2023).

2.1 Participants

The larger randomized controlled trial conducted at the Center for Man in Aviation, Royal Netherlands Airforce (RNLAf; Soesterberg, the Netherlands) was carried out in accordance with the principles outlined in the Declaration of Helsinki. The study received ethical approval from the Medical Ethical Committee Brabant (reference: NL62145.028.17/P1749) and the Surgeon General of the Ministry of Defense (reference: DGO100117022).

Informed consent was obtained from each participant. The trial was registered in the Dutch Trial Register (No. NTR6922) and EU Clinical Trials Register (No. 2017-002288-16).

Participation in this study was open to employees of the RNLAf, aged between 18 and 60 years, who met the aeromedical fitness criteria of the RNLAf Military Aviation Regulations or European Aviation Regulations (European Aviation Safety Authority EASA, 2011; Military Aviation Authority, 2020). Exclusion criteria primarily revolved around potential interactions or side effects involving caffeine or placebo, including conditions such as pregnancy or breastfeeding, usage of medications metabolized by CYP3A4/5, CYP2C19, or CYP2C9 enzymes, and psychiatric disorders (e.g., sleep disturbances).

Upon receiving comprehensive verbal and written information detailing the objectives, implications, and limitations of the trial, all participants provided written consent. This consent was given on a voluntary basis and could be withdrawn at any point without any adverse consequences. In adherence to both national and international privacy regulations, no study-related data were incorporated into the participants' medical records.

The trial included 32 subjects: two subjects did not participate in the caffeine condition due to operational reasons. According to the design protocol of the study, their test results were included in the analysis. The subjects characteristics are equal to those described in the article about the comparison between the effects of modafinil and caffeine with placebo on night-time vigilance (Wingelaar-Jagt et al., 2023): Subjects' ages ranged from 25 to 59 years (median age: 30.9 years, IQR: 28.9–39.3 years). Among the 32 subjects, five (16%) were female, and a majority of 21 (66%) were pilots. On trial days, the median waking time of the subjects was 07:00 a.m. (IQR: 06:00–07:30 a.m.), meaning that at T0 the subjects had a median period of wakefulness of 17 h (IQR: 16.5–18.0 h).

2.2 Study drugs

Caffeine is a widely accepted, available, and well-known stimulant (McLellan et al., 2016). It is a nonprescription stimulant that blocks adenosine receptors (Daubner et al., 2021). Absorption of caffeine (usually in the range of 200–600 mg) is rapid (15–40 min), and its effects are observable 15–20 min after administration (Caldwell et al., 2009). With a half-life of 4–6 h, it improves vigilance until approximately 8 h after administration (Klopping et al., 2005).

Modafinil, usually at a dose of 100–200 mg, is a newer stimulant that is already used as a fatigue countermeasure in the air forces of Singapore, the United States, India, and France (Ooi et al., 2019). It is a prescription drug, that in the United States is FDA-approved for the treatment of narcolepsy, sleep work shift disorder and obstructive sleep apnea in adults. Although its exact biochemical process is unknown, it is thought to alter the height of different neurotransmitters (e.g., serotonin, noradrenalin, dopamine, and gamma-aminobutyric acid (Kim, 2012; Battleday and Brem, 2015). Its effectiveness as a countermeasure has been demonstrated in several studies with different periods of wakefulness (Wesensten et al., 2004; Estrada et al., 2012; Wingelaar-Jagt et al., 2023).

TABLE 1 Overview of study design and data collection. All study days were identical, the only difference being the medication administered.

Timing	Activity
The 3 days before every trial day	Sleep diary
	Caffeine log
4:30 p.m.	Vital parameters
	Stanford Sleepiness Scale
	Familiarization with PVT and VigTrack
5:00 p.m.	Subject ceased caffeine consumption
6:00 p.m.	Baseline block (T-6)
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
Midnight	Second baseline block (T0)
	Vital parameters
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
	Blood samples
	Test medication administration
1:00 a.m.	First test block (T1)
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
2:00 a.m.	Second test block (T2)
	Vital parameters
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
3:00 a.m.	Third test block (T3)
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
	Blood samples
4:00 a.m.	Fourth test block (T4)
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
6:00 a.m.	Fifth test block (T6)
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
	Blood samples
8:00 a.m.	Sixth test block (T8)
	Vital parameters
	Stanford Sleepiness scale
	Assessment of VigTrack and PVT
Outtake	Blood samples
	Sleep questionnaires

Capsules that only contained a filler and no active substance were used as the placebo for comparison.

2.3 Materials

On the trial days, several parameters were measured six times: baseline measurement at 6 h (T-6) before administering trial medication (T0) and at 1, 2, 3, 4, 6 and 8 h after T0 (T1, T2, T3, T4, T6 and T8, respectively).

The Vigilance and Tracking test (VigTrack) is a dual-task that measures vigilance performance under the continuous load of a compensatory tracking task. The test has been used in various studies and is sensitive for measuring vigilance and alertness (Valk and Simons, 2009; Simons, 2017). During the tracking task, participants had to steer a blue dot using a joystick such that it remained below a red dot in the center of the display. The blue dot is programmed to move continuously from the center of the display. While tracking, participants had to perform an additional vigilance task. Inside the red dot, a black square alternated with a diamond, once per second. At random intervals, a hexagon was presented. When this occurred, participants had to press an additional key on the joystick. The duration of this test was 10 min, and primary endpoints included root mean square tracking error, percentage omissions and mean reaction time. At the start of every trial day, three familiarization sessions of 5 min were scheduled for all subjects to avoid practice bias during the actual measurements.

The PVT measures the speed with which subjects respond to a red stimulus and is used to assess the vigilance of subjects (Basner and Dinges, 2011). The inter-stimulus interval, defined as the period between the last response and the appearance of the next stimulus, varies randomly from 2 to 10 s. The duration of this test was 10 min, and primary endpoints included reaction time and lapses. Lapses (errors of omission) were defined as reaction times ≥ 500 msec. At the start of every trial day, a familiarization session of 5 min was scheduled for all subjects to avoid practice bias during the actual measurements.

The Stanford Sleepiness Scale (SSS) was used to subjectively assess the degree of sleepiness in subjects during the test days (Hoddes et al., 1973). This subjective rating scale is sensitive to detect any significant increase in sleepiness or fatigue, and is highly correlated with flying performance and the threshold of information-processing speed during periods of intense fatigue (Perelli, 1980).

2.4 Design

The randomized controlled trial encompassed a series of three nonconsecutive trial days for each subject, during which capsules of modafinil, caffeine, or placebo were administered once immediately after midnight. Details of the trial days can be found in Table 1 and a previously published article by Wingelaar-Jagt et al. (2023). The modafinil dosage administered was 200 mg, a recognized effective fatigue mitigation measure for military aviators (Caldwell et al., 2000; Caldwell et al., 2009). The dosage of caffeine (300 mg) corresponded to the standard dosage presently administered to RNLAf aviators, representing a

medium-range yet efficacious amount (Lohi et al., 2007; Caldwell et al., 2009).

A wash-out interval of no less than 7 days, as advised by our pharmacist, was instituted to ensure complete drug elimination and to prevent any interference with subsequent trial day analyses. The trial was double-blinded to ensure that both participants and investigators remained uninformed about the treatment assigned on trial days. The sequence of treatments (placebo, caffeine, or modafinil) for each individual was determined through a computer-generated randomization schedule, organized and overseen by an external statistician. This randomization encompassed all feasible (six) treatment sequences, thus promoting equilibrium in terms of carryover effects; factors like skill enhancement or learning bias on the test battery. In preparation for each trial day, researchers obtained a treatment kit from the pharmacist, featuring capsules that were identical and labeled with the respective subject number and trial day.

2.5 Procedure

In the week leading up to each trial day, participants adhered to the local time zone of the research center (daylight saving GMT +2) to preemptively counter the potential influence of jetlag, which could introduce confounding variables to the test outcomes. Throughout the trial days, participants were instructed to refrain from engaging in strenuous physical activities, including sports, and from sleeping. They diligently maintained a record of their activities and documented their caffeine consumption. Regular consumption of their habitual amount of caffeine-containing products was permitted up until 5:00 p.m. To prevent caffeine from affecting vigilance, participants refrained from further caffeine intake after 5:00 p.m. on trial days.

Vital parameters such as temperature, blood pressure, and pulse were assessed on four occasions during each trial day: twice before the administration of medication, and at two and eight h post-administration (refer to Table 1 for details). In addition, female subjects underwent pregnancy tests on each trial day, and all participants were queried about any recent usage of concomitant medications or any unauthorized substances within the preceding 3 days. Participants were inquired about any adverse events multiple times during the course of the trial days and at each visit post-screening. Any adverse events that occurred during the study were recorded.

2.6 Statistical analysis

Differences of baseline characteristics (age, sex, function, waking time and wakefulness time) were tested using the Student's t-test or Kruskal–Wallis test where appropriate.

Responses in the aforementioned tests (VigTrack, PVT and SSS) were collected during the night. An area under the curve (AUC) based on the results during the test night was calculated for each of these parameters, using the delta score. The delta score is corrected for the baseline scores at T-6 of each test subject (thus; Delta score = score at the respective test moment – the score of that individual at T-6).

TABLE 2 Comparison of characteristics of the three fatigue groups.

	Missed caffeine administration	Female	Median age	Median waking time	Median period of wakefulness at T0
Total (n = 32)	2 (6%)	5 (16%)	30.9 years (IQR: 29–39)	07:00 a.m. (IQR: 06:00–07:30)	17.0 h (IQR: 16.5–18.0 h)
Fatigue-resistant (n = 11)	1 (9%)	1 (9%)	31.4 years (IQR: 30–50)	07:20 a.m. (IQR: 06:12–07:30)	16.7 h (IQR: 16.5–17.8 h)
Fatigue-intermediate (n = 10)	0 (0%)	0 (0%)	29.2 years (IQR: 28–33)	06:57 a.m. (IQR: 06:00–07:30)	17.0 h (IQR: 16.5–18.0 h)
Fatigue-vulnerable (n = 11)	1 (9%)	4 (36%)	33.0 years (IQR: 30–36)	06:35 a.m. (IQR: 06:15–07:00)	17.4 h (IQR: 17.0–17.8 h)

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (Armonk, NY: IBM Corp, 2020). A univariate factorial analysis of variance (ANOVA) using the AUC was conducted to analyze the effects of group (F_{VUL} , F_{INT} , and F_{RES}) and treatment (modafinil, caffeine, and placebo), and the interaction thereof. When the ANOVA revealed a significant effect, Tukey's HSD *post hoc* test was utilized to analyze the difference between the different treatments or groups. A p -value <0.05 was considered statistically significant.

3 Results

The administration of the drugs did not exert any discernible impact on the subjects' vital parameters. Throughout the trial, no adverse events were reported. The trial concluded in alignment with the protocol.

3.1 Characterization of fatigue resistant and fatigue vulnerable individuals

On the placebo test night, 224 PVT tests were performed by all subjects from T0 to T8. The Kolmogorov-Smirnov and Shapiro-Wilk tests of these data yielded p -values <0.001 , indicating that these data were non-normally distributed. The median number of lapses was 13 (IQR: 6–24, range: 0–60).

To define participants as fatigue-resistant or -vulnerable, the average numbers of PVT lapses scored at T0 until T8 (h 17–25 of the sleep deprivation) during the placebo night were ranked. The fatigue-vulnerable (F_{VUL}) group was defined as the lowest scoring third of participants, the fatigue-resistant (F_{RES}) group as the highest scoring third, and the fatigue-intermediate (F_{INT}) group as participants in between. In the case of ties, participants were placed in the better scoring group. This classification gave the following number of participants in each group: F_{VUL} , $n = 11$; F_{INT} , $n = 10$; and F_{RES} , $n = 11$.

Of the 11 fatigue-resistant participants, one missed the caffeine administration, similar to the F_{VUL} group. Median age was higher in the F_{VUL} group than in the F_{RES} group, and fatigue-vulnerable participants had a slightly longer period of wakefulness at T0. The baseline characteristics of the three groups are shown in

Table 2. Sex, age, and waking time (and derived period of wakefulness) did not significantly differ between the F_{VUL} , F_{INT} , and F_{RES} groups according to the Kruskal–Wallis test, with p -values of 0.329, 0.194, and 0.647, respectively.

3.2 Effect of fatigue group on treatment effects

The mean AUC of outcome parameters according to treatment and fatigue group are shown in Figure 1. The results of univariate factorial ANOVAs and subsequent *post hoc* tests are displayed in Table 3.

For most parameters, except for the VigTrack mean tracking error and mean percentage omissions, there was a significant main effect of treatment. For the majority of the significant results, the subsequent *post hoc* tests showed that outcomes were significantly better after modafinil and caffeine administration than after placebo administration.

There was no significant main effect of fatigue group for SSS or VigTrack mean tracking error; the main effect of fatigue group was significant for the other four parameters. Subsequent *post hoc* tests revealed that scores were significantly better in the F_{INT} and F_{RES} groups than in the F_{VUL} group. There were no significant differences between the F_{INT} and F_{RES} groups.

There was a significant interaction effect between treatment and fatigue group for PVT number of lapses. This indicates that for this parameter the treatment did have a significantly different effect depending on the fatigue group. This is congruent with Figure 1B, in which the performance of the F_{VUL} group seems to be steadily lower than that of the F_{INT} and F_{RES} groups. This was especially pronounced after placebo administration. Furthermore, the effect of modafinil and caffeine administration appeared to be more extensive on scores in the F_{VUL} group than in the F_{INT} and F_{RES} groups. These trends in Figure 1 are comparable for most parameters (except for the SSS). For the PVT mean reaction time and VigTrack parameters, the scores in the F_{VUL} group after modafinil or caffeine administration were even similar to (or worse than) those in the F_{INT} and F_{RES} groups after placebo administration. However, the univariate factorial ANOVAs showed no significant interaction effect between treatment and fatigue group for the other parameters.

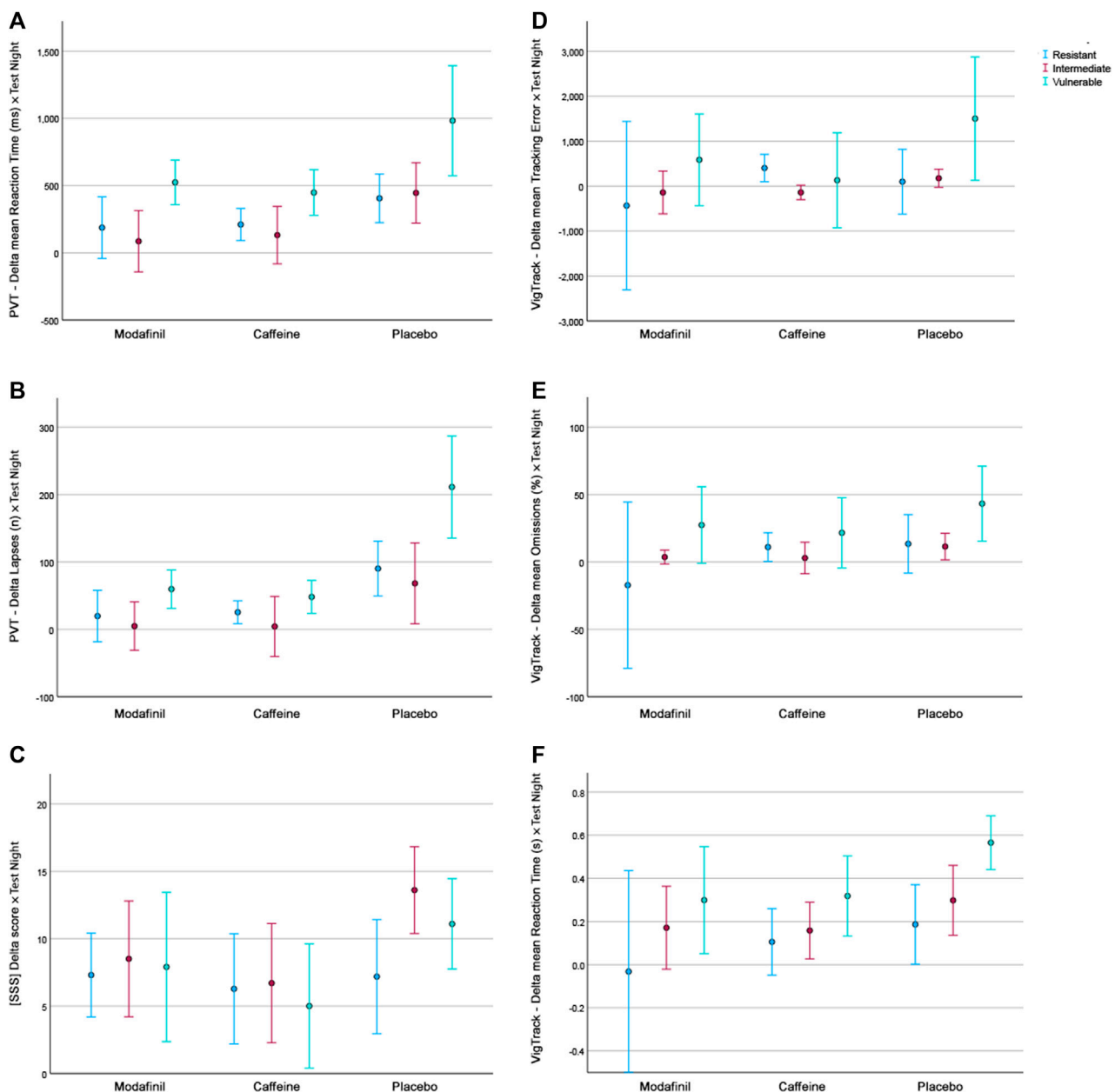


FIGURE 1

The mean AUC of outcome parameters according to treatment and fatigue group. (A). PVT–Delta mean Reaction Time. (B). PVT–Delta Lapses. (C). Delta SSS scores. (D). VigTrack–Delta mean Tracking Error. (E). VigTrack–Delta mean Percentage Omissions. (F). VigTrack–Delta mean Reaction Time. Blue = fatigue-resistant group, red = fatigue-intermediate group, green = fatigue-vulnerable group.

4 Discussion

This study demonstrates that individuals with different fatigue tolerances react differently to the negative effects of a limited period of sleep deprivation on performance. The classification of fatigue tolerance according to PVT lapses when sleep-deprived seems to be able to predict this. In a previously published manuscript about this trial, we concluded that subjects administered modafinil or caffeine showed greater vigilance after an extended period of continuous wakefulness than those administered a placebo (Wingelaar-Jagt

et al., 2023). The current study indicates that the extent to which stimulants improve performance might depend on the fatigue tolerance of the individual. Individuals with a low fatigue tolerance (i.e., fatigue-vulnerable individuals) seem to benefit more from stimulant administration, while individuals who are fatigue-resistant or -intermediate generally retain higher performance than the fatigue-vulnerable individuals, regardless of the intervention.

PVT lapses during sleep deprivation showed strong interindividual differences in our study, in line with the literature (Van Dongen et al., 2004; Chua et al., 2019). Congruent with previous

TABLE 3 Outcomes of the Univariate factorial ANOVAs.

Covariates		PVT–mean reaction time	PVT–number of lapses	SSS	VigTrack–mean tracking error	VigTrack–mean percentage omissions	VigTrack–mean reaction time
Main effect of treatment		$F(2, 9) = 11.448, p < 0.001^a$	$F(2, 9) = 24.101, p < 0.001^a$	$F(2, 9) = 4.829, p = 0.010^a$	$F(2, 9) = 1.546, p = 0.219$	$F(2, 9) = 1.680, p = 0.192$	$F(2, 9) = 3.464, p < 0.036^a$
Pairwise comparisons	modafinil vs. placebo	$p < 0.001^a$	$p = 0.036^a$	$p < 0.001^a$	n.a	n.a	$p = 0.200$
	caffeine vs. placebo	$p < 0.001^a$	$p = 0.130$	$p < 0.001^a$	n.a	n.a	$p = 0.009^a$
Main effect of fatigue group		$F(2, 9) = 15.894, p < 0.001^a$	$F(2, 9) = 13.680, p < 0.001^a$	$F(2, 9) = 1.566, p = 0.215$	$F(2, 9) = 3.021, p = 0.054$	$F(2, 9) = 4.911, p = 0.010^a$	$F(2, 9) = 7.444, p < 0.001^a$
Pairwise comparisons	vulnerable vs. intermediate	$p < 0.001^a$	$p = 0.060^a$	$p < 0.001^a$	n.a	$p = 0.038^a$	n.a
	vulnerable vs. resistant	$p < 0.001^a$	$p < 0.001^a$	$p < 0.001^a$	n.a	$p = 0.016^a$	n.a
	intermediate vs. resistant	$p = 0.829$	$p = 0.317$	$p = 0.431$	n.a	$p = 0.953$	n.a
Interaction effect		$F(4, 9) = 0.797, p = 0.530$	$F(4, 9) = 0.317, p = 0.866$	$F(4, 9) = 2.528, p = 0.046^a$	$F(4, 9) = 1.156, p = 0.336$	$F(4, 9) = 0.642, p = 0.634$	$F(4, 9) = 0.913, p = 0.460$

^aStatistically significant results ($p < .05$) from the Univariate factorial ANOVA, or subsequent Tukey HSD, *post hoc* tests.

studies, we split the participants into three groups based on the number of participants after ranking their performance (Chua et al., 2019; Caldwell et al., 2020; Galli et al., 2022). However, the number of groups in previous studies varied between two and four, resulting in different cut-off values for the groups. These different classifications of fatigue vulnerability make it difficult to compare the results. While the three fatigue groups were statistically comparable at baseline, the median period of wakefulness was slightly longer in the F_{INT} and F_{VUL} groups than in the F_{RES} group. This is similar to a finding of Caldwell et al., who found a non-statistically significant difference in hours slept in the three nights prior to the test. However, low-scoring performers had obtained more hours of sleep in their study (Caldwell et al., 2020).

In concordance with previous research, we found that fatigue tolerance classification through PVT lapses when sleep-deprived seems to be valid (Patanaik et al., 2015; Chua et al., 2019; Yamazaki et al., 2022). The fatigue group had a significant effect on the majority of the parameters, with the exception of SSS and VigTrack mean tracking error, with the latter p -value approaching 0.05. The current study showed a significant interaction effect between treatment and fatigue group for PVT number of lapses. This indicates that for this single parameter the treatment did have a significantly different effect depending on the fatigue group. This is congruent with Figure 1, in which for all parameters (except for the SSS) the performance of the F_{VUL} group was consistently worse than that of the F_{INT} and F_{RES} groups. However, the ANOVAs showed no significant interaction effect between treatment and fatigue group for the other parameters. This discrepancy between the findings of the univariate factorial ANOVAs and visual depiction of the mean AUC of the different parameters according to the treatment and fatigue group may be because the direction of the effect of treatment is similar

for the three fatigue groups. As Figure 1 indicates that the effect of modafinil and caffeine administration on scores appeared to be more extensive in the F_{VUL} group than in the F_{INT} and F_{RES} groups (except for the SSS), it might solely be the size of the effect that is different. Naturally, as the F_{VUL} group had a lower performance after placebo administration, there is more room in this group for performance improvements due to stimulant administration than in the F_{INT} and F_{RES} groups. This discrepancy is not as pronounced in our study as it was in that of Caldwell et al., who reported that high-performing individuals did not benefit substantially from modafinil administration while low-performing individuals did (Caldwell et al., 2020). However, for the PVT mean reaction time and VigTrack parameters, scores in the F_{VUL} group after modafinil or caffeine administration were similar to (or worse than) those in the F_{INT} and F_{RES} groups after placebo administration. This suggests that even though modafinil and caffeine improve performance, regardless of fatigue tolerance, performance of F_{VUL} individuals remain lower after stimulant administration than that of F_{RES} individuals without stimulants. This raises the question whether fatigue tolerance should be part of the selection process for individuals who regularly have to perform while fatigued (like military pilots on deployment).

Naturally, this study has some limitations. First, there is possible selection bias; the subjects were all military, aeromedically screened, and predominantly young. This is the population of interest for the Royal Netherlands Air Force, but this makes the results difficult to extrapolate to the general population. Furthermore, even though there was high motivation among our population to participate in this study, individuals who are uncomfortable with staying awake an entire night (possibly because they are fatigue-vulnerable) might be less inclined to participate in a sleep deprivation study. Second, the lack of a standard method and classification of fatigue groups makes

it difficult to compare this research with previous studies. It would be favorable to introduce a classification including cut-off values that can be used in future studies to identify fatigue-resistant and -vulnerable individuals in order to increase comparability. Third, this study was performed in a controlled laboratory environment and used relatively simple tasks such as the PVT and VigTrack. Although both tests are sensitive for measuring vigilance and alertness, the results cannot be simply extrapolated to real-life scenarios because the workload and complexity of tasks in the cockpit are of a different caliber, which might influence individuals' reactions to fatigue (Caldwell and Roberts, 2000; Ehlert and Wilson, 2021). Lastly, this study induced a rather limited duration of total sleep deprivation. Although research suggests that fatigue tolerance is consistent across different types of sleep deprivation, these findings might not accurately predict the response to other types of sleep deprivation, like chronic sleep restriction.

In conclusion, this study shows that fatigue tolerance classification through PVT lapses when sleep-deprived seems to predict the performance of other psychometric parameters of individuals when sleep-deprived. The importance of fatigue and its negative effects on performance is not limited to (military) aviation. In industries such as healthcare and logistics, in which peak performance is required during night-time or after periods of sleep deprivation, it is equally important to be able to identify which individuals might be at risk of performance decrements. To harmonize research into fatigue vulnerability, the identification of fatigue tolerance groups must be standardized and the introduction of a classification including cut-off values is paramount. The present study confirms that individuals have different degrees of performance degradation during a limited period of sleep deprivation and that, depending on the fatigue tolerance of the subject, stimulants might correct this to different extents. Stimulants might be especially useful for fatigue-vulnerable individuals, even though their performance after stimulant administration may remain lower than that of fatigue-resistant individuals when sleep-deprived.

Data availability statement

The datasets presented in this article are not readily available because of policy and privacy restrictions. Requests to access the datasets should be directed to the corresponding authors.

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Ethics statement

The studies involving humans were approved by Medical Ethical Committee Brabant (reference: NL62145.028.17/P1749) and the Surgeon General of the Ministry of Defense (reference: DGO100117022). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

YW-J: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing—original draft, Writing—review and editing. TW: Data curation, Formal Analysis, Investigation, Validation, Writing—review and editing. WR: Conceptualization, Supervision, Writing—review and editing. JR: Conceptualization, Supervision, Writing—review and editing.

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Conflict of interest

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The sex effect on balance control while standing on vestibular-demanding tasks with/without vestibular simulations: implication for sensorimotor training for future space missions

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Background: Anatomical differences between sexes in the vestibular system have been reported. It has also been demonstrated that there is a sex difference in balance control while standing on vestibular-demanding tasks. In 2024, NASA expects to send the first female to the Moon. Therefore, to extend the current knowledge, this study attempted to examine whether different sexes respond differently to vestibular-disrupted and vestibular-demanding environments.

Method: A total of fifteen males and fifteen females participated in this study. The vestibular function was quantified through different SOT conditions (SOT1: baseline; SOT5: vestibular demanding by standing with blindfolded and sway reference surface). The vestibular stimulation (VS) was applied either unilaterally or bilaterally to vestibular system to induce the sensory-conflicted and challenging tasks. Thus, a total of 6 conditions (2 SOT conditions X 3 VSs: no-VS, unilateral VS, and bilateral VS) were randomly given to these participants. Three approaches can be quantified the balance control: 1) the performance ratio (PR) of center of gravity trajectories (CoG), 2) the sample entropy measure (SampEn) of CoG, and 3) the total traveling distance of CoG. A mixed three-way repeated ANOVA measure was used to determine the interaction among the sex effect, the effect of SOT, and the effect of VS on balance control.

Results: A significant sex effect on balance control was found in the PR of CoG in the anterior-posterior (AP) direction ($p = 0.026$) and in the SampEn of CoG in both AP and medial-lateral (ML) directions ($p = 0.025$, $p < 0.001$, respectively). Also, a significant interaction among the sex effect, the effect of SOT, and the effect of VS on balance control was observed in PR of CoG in the ML direction ($p < 0.001$), SampEn of CoG in the AP and ML directions ($p = 0.002$, $p < 0.001$, respectively), and a traveling distance in AP direction ($p = 0.041$).

Abbreviations: SOT, sensory organization test; CoG, center of gravity; PR, Performance ratio; SampEn, Sample Entropy; AP, anterior-posterior; ML, medial-lateral; VS, vestibular stimulation; N, no vestibular stimulation; Uni, unilateral vestibular stimulation; Bi, bilateral vestibular stimulation.

Conclusion: The findings in the present study clearly revealed the necessity to take sex effect into consideration while standing in vestibular-perturbed or/and vestibular demanding tasks. Also, the results in the present study could be a fundamental reference for future sensorimotor training.

KEYWORDS

vestibular stimulation, sensory organization test, balance control, standing, mastoid vibration

1 Introduction

On Earth, humans are capable of detecting gravity, orienting themselves to their surroundings, and performing sensory motor activities, such as walking and standing in the dark or on slippery, uneven, or foamy surfaces, without any hesitation. A vestibular system plays an important role in detecting head rotation, acceleration, and self-motion transitions in relation to gravity in the above-mentioned circumstances (Messina et al., 2021). Also, when the head moves, the vestibular ocular reflex maintains the stability of the eyes in inertial space, so that the retinal image of the fixed visual surround appears to be stable, regardless of the motion of the head (Martines et al., 2021). It should be noted, however, that standing or walking in microgravity or at varying levels of gravity may result in different vestibular responses to maintain balance control. A prime example is Dr. Harrison Schmitt, an astronaut on the Apollo 17 mission, who fell several times and encountered difficulties in getting up from the Moon's surface due to the fluctuating levels of gravity while picking samples (https://www.youtube.com/watch?v=Ke65jU_yYso, assessed on 5 November 2023). Moreover, Jain et al. (2010) and Wood et al. (2015) examine vestibular-related balance control in 11 crew members prior to and after spaceflight (11–13 days short-duration shuttle spaceflights) and suggest that alternate gravity temporarily impairs the vestibular system, which causes misinterpretations of the central nervous system and causes imbalances when astronauts stand or walk. The question may arise as to whether there is a sex difference in vestibular function when standing in a vestibularly disrupted environment.

Males and females have physiological and anatomical differences when it comes to the vestibular system (Bowman et al., 2000; Corazzi et al., 2020; Lien and Yang, 2021; El Khiali et al., 2022). In particular, it has been shown that female cochlea is shorter than male cochlea, resulting in a stiffer basilar membrane (Corazzi et al., 2020). Consequently, this anatomical sex difference in the basilar membrane may further influence the perception of vestibular signals (Bowman et al., 2000). It has been demonstrated that females exhibit higher amplitudes of ocular vestibular-evoked myogenic potentials and superior horizontal semicircular canal function than males, which results in a higher sensitivity to vestibular signal perception in females than males under air-conducted sound, bone-conducted vibration, and galvanic vestibular stimulation (Sung et al., 2011; Battersby, 2019; Schubert et al., 2022). In females, this increased sensitivity to vestibular-related perception may lead to the possibility of an imbalance when performing vestibular-demanding tasks, such as standing on a foam surface and closing their eyes. Vereck et al. (2008) and Wolfson et al. (1994) support this abovementioned

hypothesis by showing that the sex effect (302 females vs. 250 males) has a significant effect on the vestibular system in controlling balance while standing in different vestibular-demanding environments. In particular, numbers of females adopt a stepping strategy (step over the platform because of losing balance). In general, females demonstrated worse balance control than males while standing in vestibular-demanding tasks, such as standing with eye-closed and a single leg on the foam surface, standing with eye-closed and both legs on the foam surface, or standing with eye-closed and both legs on sway-reference surface (Sensory Organization Test condition 5, SOT5). NASA plans to send its first female astronaut to the Moon in 2024 as part of its Artemis program and plans to send more female astronauts to space missions in the years to come. According to the studies, it seems that females have a tendency to be fall while standing in a vestibular-demanding environment. It is essential to gain a better understanding of how the vestibular-related balance control differs in men and women when standing in a disrupted vestibular environment in order to develop sensorimotor training programs that will prevent falls among female astronauts in the future.

As part of clinical assessment (Black et al., 1989; Goebel and Paige, 1989; Hytönen et al., 1989; Mulavara et al., 2013), the SOT has frequently been employed to assess the vestibular function in patients with various vestibular disorders by simultaneously disturbing both the visual system (closed eyes) and the somatosensory system (sway-reference surface). Despite being constructed approximately 30 years ago, this SOT remains in use in the present time to assess vestibular function in astronauts immediately following spaceflight (11–13 days short-duration shuttle spaceflights, Ozdemir et al., 2018) and to assess whether 48 astronauts recovered balance control after prolonged spaceflight (approximately 6 months, Tays et al., 2021; Shishkin et al., 2023). According to the findings, staying in microgravity for a long period of time requires at least 30 days in order to fully restore balance control due to the adaptation and re-adaptation of the vestibular system between different level of gravity (Tays et al., 2021; Shishkin et al., 2023). For SOT, the equilibrium scores are used to quantify the vestibular function by measuring the movement of the center of gravity primarily forward and backward (Black et al., 1989; Goebel and Paige, 1989; Hytönen et al., 1989; Mulavara, 2013; Vanicek et al., 2013). Specifically, the limit of stability is approximately seven degrees (posteriorly) and five degrees (anteriorly, Vanicek et al., 2013). Participants who step off from the platform will receive an equilibrium score of 0 (failure equilibrium score, Vanicek et al., 2013). In this regard, however, it raises three concerns about this measure of equilibrium score: 1) the ceiling effect, 2) the sensitivity, and 3) the neglect of balance control in the ML direction. Also, it is important to note that even in patients with known vestibular

lesions, the measure of equilibrium score in SOT is only about 50% sensitive to vestibular loss (Mishra et al., 2009). It is therefore important to use the equilibrium score measure cautiously in the evaluation of vestibular function since it may result in an incorrect interpretation of the sex effect on vestibular-related balance control. It may explain why a study have found no statistical differences between sexes in vestibular-related balance control using the measure of equilibrium score in SOT (Faraldo-García et al., 2011). Interestingly, this study still suggest that the sex effect should be taken into account when determining vestibular function because women use ankle strategies more than men when performing a vestibular-demanding task (Faraldo-García et al., 2011). Therefore, one of aims in present study was to assess balance control using other three practical measurements rather than the equilibrium score to determine the sex effect on vestibular system as follows: performance ratio of movement in the center of gravity (CoG), total traveling distance of CoG, and the complexity of movement of CoG using entropy measure.

The performance ratio (PR) is used to identify the degree of balance control (center of gravity, CoG) sway in the anterior-posterior (AP) and medial-lateral (ML) directions and is calculated by the numerical integral of the rectified CoG sway signal scaled to be a fraction of the maximum sway amplitude while standing on normal or perturbed environment (Nashner et al., 1982). This PR has been used to differentiate the patients with different types of vestibular deficits (Black et al., 1989; Nashner and Peters, 1990). In short, a greater PR reflects a greater sum of instantaneous sway, indicating a greater reliance on the vestibular system to maintain balance while performing a vestibular-demanding task. The total traveling distance of the CoG can simply be defined as the distance the CoG travels in a given period of time. A longer traveling distance commonly be interpreted as a worse balance control. For over a decade, the concept of entropy has been widely used to describe the complexity of physiological signals through time series analysis (Richman and Moorma, 2000; Richman et al., 2004; Donker et al., 2007; Hansen et al., 2017; Montesinos et al., 2018; Blazkiewicz et al., 2021; Fischer et al., 2023). Compared to conventional calculations in sway changes in means and standard deviations, analyzing the sway data in time series can provide another aspect of balance controls in uses in degree of freedom and understand the underlying causes of trends or systemic patterns over time. A sample entropy (SampEn) method has the following advantages: 1) SampEn has a better data length independence, 2) SampEn has better anti-noise capacity, and 3) SampEn is suitable for short datasets (Richman and Mooram, 2000; Montesinos et al., 2018). In light of the differences in SampEn values, it is likely that executing different types of movements in time series requires a different degree of freedom. A more irregular movement (greater SampEn value) is commonly observed for adapting to the complex (sensory-conflicted) environment (Jia et al., 2017; Chen et al., 2021). In particular, patients with various vestibular dysfunction, no matter whether they stand on a solid or compliant surface, have a greater SampEn value than healthy controls (Lubetzky et al., 2018). Also, in these patients with vestibular dysfunction, SampEn values are even greater when standing on compliant surfaces than on solid surfaces (Lubetzky et al., 2018), requiring higher degree of freedoms in movements to control balance.

A large, well-developed facility such as NASA, for example, has the capability of measuring the changes in vestibular-related balance control between sexes in response to gravity changes; however, these costs cannot be justified in a typical biomechanical laboratory. There is, however, a feasible and cost-effective method of determining sex differences in vestibular-related balance control under vestibular-perturbed and vestibular-demanding environment by using vestibular stimulation (Kavounoudias et al., 1999; Lin et al., 2022). Specifically, applying VS increases the CoG sway area in both young (Lin et al., 2022) and older adults (Lin et al., 2022); furthermore, applying bilateral VS increased even more CoG sway area than applying unilateral VS in older adults (Lin et al., 2022), indicating that different types of VS induced different balance controls. The use of such a VS paradigm would mimic an unpredictable and vestibular-perturbed environment, which necessitates greater reliance on the vestibular system for the maintenance of balance. Thus, one of the aims of this study was to apply this paradigm to determine the sex differences in vestibular system for maintaining the vestibular-related balance control.

With the use of VS and SOT, this study was supported by NASA and attempted to meet NASA's current focus on understanding the sex effect on vestibular-related balance controls while standing in normal and vestibular-demanding environments. This study expected to observe that 1) a sex effect was found on balance control, regardless of whether VS was administered or what SOT conditions participants were in, with females achieving worse balance control but experiencing higher degrees of freedom of control; 2) whether or not VS was given, there was a interaction between sex effect and SOT condition effect on balance control, 3) no matter what SOT conditions participants stood in, the balance control of females and males responded differently to VS, and 4) while standing in vestibular-demanding and bilaterally vestibular-perturbed condition (the most challenging task), female might demonstrate worse balance control and greater levels of degree of freedom in balance control than males compared to other conditions.

2 Materials and methods

2.1 Participants

In total, thirty healthy participants attended in this study (15 males and 15 females, age: 34.93 ± 17.36 years old, height: 170 ± 7.19 cm, weight: 68.17 ± 12.13 kg). To recruit these healthy adults, a variety of advertising methods were employed, including flyers posted on university campuses and in local community centers, as well as an online bulletin posted on the university's website. All healthy adults were required to meet the following inclusion criteria: 1) all participants must be free of musculoskeletal deficits and have no history of extremity injuries, 2) participants must not have any joint surgeries that would affect their gait pattern, 3) participants must pass the dizzy handicap inventory (score = 0), indicating that potential vestibular dysfunction may not exist, and 4) participants never experienced any type of vestibular stimulation. The exclusion criteria were that 1) these healthy adults had any type of vestibular diseases or vestibular surgeries, 2) these healthy adults had any type of neurological disorders, and 3) participants scored

below 23 in the Mini Mental State Examination, indicating the potential cognitive impairments (Foreman et al., 1996). This study was approved by the Institutional Review Board at the University of Nebraska Medical Center (IRB Protocol # 379-17-EP). The data collection only began while participants voluntarily signed the inform consent.

2.2 Experimental setup

A Balance Master System 8.4 (NeuroCom International Clackamas, OR, United States) was applied to identify the vestibular function through the sensory organization test. This system included a moveable visual surround and a support surface that could rotate around the ML axis led participants to lean forward (the maximum range was approximately 7°) or backward (the maximum range was approximately 5°) in the AP direction (Nashner and Peter, 1990). Two force plates (22.9 cm × 45.7 cm) were connected by a pin joint and used to record the displacement of center of gravity (CoG) at the sampling frequency of 100 Hz. The sensory organization test (SOT) contained a total of 6 conditions to identify the functions of visual, somatosensory, and vestibular systems (Black et al., 1989). In this study, only SOT-1 (baseline, stationary-platform, full visual support), and SOT-5 (sway-reference platform, eye-closed) were used to identify the effect of different vestibular stimulations on balance control during standing in normal and the vestibular-demanding tasks. Specifically, this SOT-5 has been widely used to probe the vestibular contributions to balance control in healthy controls (Hamid et al., 1991; Ford-Smith et al., 1995), in older adults and fallers (Horak et al., 1989), in patients with vestibular dysfunction (Di Fabio, 1995), and in astronauts (Tays et al., 2021; Shishkin et al., 2023).

In this study, mechanical vibrotactile stimulation (VS) was generated by placing two electromechanical vibrotactile transducers (EMS2 tactors; Engineering Acoustics, FL, United States) to the mastoid processes bilaterally. Participants can readily perceive the vibrations that occur through the use of these tactors, since they are designed to be mounted within a seat or cushion. With a rise time of 25 milliseconds, the EMS2 tactor produces large displacements even when applied against the mechanical impedance of the body. A maximum peak-to-peak displacement of 2 mm was recorded when the device was loaded. Tactors were 18.8 mm in height and 24 g in weight. Tactors had a diameter of 48.5 mm (Figure 1). The frequency of these two mastoid vibrations was set at 100 Hz and was controlled by software (TAction Creator, Engineering Acoustics, FL, United States). Applying this 100 Hz vibration has been proved to induce the slow-phase velocity of eye movement toward the vibrated side of mastoid process (Park et al., 2007). Vibration amplitudes were set at 130% of participants' minimum perceived amplitudes (Lu et al., 2022). Participants were instructed to stand still while an experimenter adjusted the vibration amplitude through the commercial software TAction Creator until they were able to perceive the minimum perceived amplitude. It was an impulse type of vibration activation, indicating an activation period of 0.5 s and a deactivation period of 0.5 s. A purpose of using this type of impulse vibration was to reduce vestibular saturation (Lu et al., 2022).

2.3 Experimental protocol

The data collection was performed at Clinical Movement Analysis Laboratory at the University of Nebraska Medical Center. Dr. Li Zheng as an exchanged scholar and Dr. Jung Hung Chien collected, processed, and analyzed the data. Before the data collection, each participant needed to fill the Mini Mental State Examination. If the individual's score of Mini Mental State Examination below 23, the experiment was terminated. During one visit, a total of six standing trials (SOT1-N: normal standing on the fixed surface without any VS, SOT1-Bi: normal standing on the fixed surface with bilateral VS, SOT1-Uni: normal standing on the fixed surface with unilateral VS, SOT5-N: standing on sway-reference surface and was blindfolded without any VS, SOT5-Bi: standing on the sway-reference surface and was blindfolded with bilateral VS, and SOT5-Uni: standing on the sway-reference surface and was blindfolded with unilateral VS) were randomly provided to each participant. The randomization procedures were as follows. Firstly, conditions SOT1-N, SOT1-Bi, SOT1-Uni, SOT5-N, SOT5-Bi, and SOT5-Uni were labeled as conditions 1, 2, 3, 4, 5, and 6. Then, the RANDBETWEEN formula built in Microsoft Excel (Microsoft, Seattle, WA, United States) was a method to select a range of numbers (1–6) to use in the randomizing process. Each trial lasted for 90 s (Chien et al., 2014). Participants' feet were placed according to the method described in Vanicek et al. (2013). Participants were instructed to stand upright on the two force plates (one for each foot) without shoes, and to place their feet according to their height. The ankles of the participant should be aligned with the thick horizontal line running through the axis of rotation of the force plate. This can be achieved by aligning the experimenter's thumb with the participant's medial malleolus and the experimenter's fingers with the horizontal line. Following this, the participant should place the outside of their heels on the vertical line marked by the letter "T" on the surface of the force plate. Also, these participants were instructed to keep their arms relaxed at their sides throughout each data collection. To ensure consistency between participants, the unilateral VS was administered through the tactor placed on the right mastoid process. Between trials, a one-minute of mandatory sitting rest was assigned (Lin et al., 2022). After 1 min rest, participants were asked to perform sit-to-stand and to walk 6 m straightly. Then, a short questionnaire, Niigata Persistent Postural-Perceptual Dizziness questionnaire (Yagi et al., 2019) was administered to each participant at the end of each trial to assess whether they experienced any uncomfortable sensations after this standing trial. The question #Q1, #Q3, #Q6, and #Q7 were selected in this questionnaire as follows: Q1) Quick movements such as standing up or turning your head, Q3) Walking at a natural pace, Q6) Sitting upright in a seat without back and arm support, and Q7) standing without touching fixed objects. Participants were asked "please indicate your answer by circling a Yes or No that best describe the extent to which you feel any discomfort or dizziness during or after the experimental trial." The experiment was terminated if the answer from this questionnaire was filled as "Yes," or participants felt any discomfort during any of the standing conditions. A data collection took approximately one and a half hours.

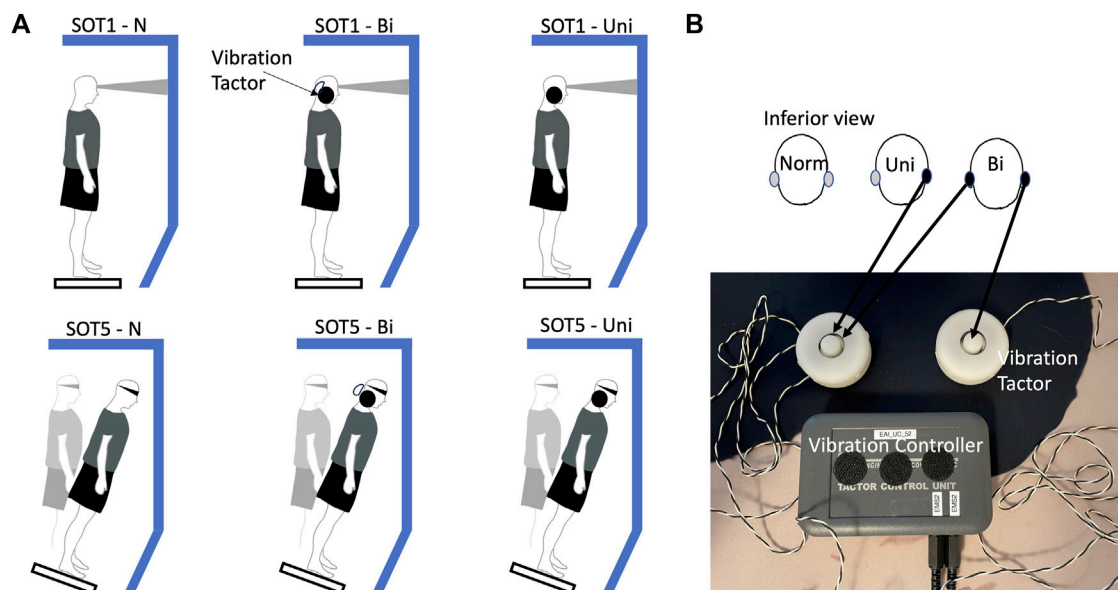


FIGURE 1
The experimental paradigm (A) the sensory organization test (B) the vestibular stimulation equipment.

2.4 Data analysis

Three types of measures in the present study were used to evaluate the balance control as follows: The total traveling distance (Lemay et al., 2014), Performance Ratio (Nashner et al., 1982; Chien et al., 2014), and Sample Entropy (Montesinos et al., 2018).

2.4.1 Total traveling distance of CoG

A total traveling distance was the sum of CoG moving distance between two time points (e.g., the CoG distance from the zero to the 0.01 s, and from the 0.01 s to the 0.02 s and so on). The total traveling distance of CoG was calculated in both AP and ML directions.

$$\text{Total Traveling Distance of CoG} = \sum_{\text{time}=0s}^{\text{time}=90s} |\text{CoG}_{\text{time}+0.01s} - \text{CoG}_{\text{time}}|$$

2.4.2 Performance ratio of CoG (PR)

Using the numerical integral of the rectified sway signal (removed from the steady-state offset) and scaling the results as a percentage of maximum sway during standing, a PR was determined (Nashner et al., 1982). Before data collection was given, participants need to stand on force plates with eye-opened and fixed surface for 10 s. The CoG coordinates in AP and ML directions in these 10 s were averaged as the CoG_{steady_state}. Then, participants were instructed to lean forward, backward, lateral-toward-right or lateral-toward-left as possible as they can before taking a step. Therefore, CoG_{max} in the AP direction was defined as range of the maximum lean forward (anterior direction) and the maximum lean backward (posterior direction) before taking a step. Also, CoG_{max} in the ML direction was defined as range of the maximum lateral-toward-right and the maximum lateral-toward-left before taking a step. PR values approaching

100 indicate a loss of balance, whereas PR values approaching zero indicate stable postural control. Also, if participants stepped off from the force plates, PR values was assigned as 100 immediately.

$$PR = \sum_{\text{time}=0s}^{\text{time}=90s} \frac{|\text{CoG}_{\text{time}} - \text{CoG}_{\text{steady_state}}|}{\text{CoG}_{\text{max}} - \text{CoG}_{\text{steady_state}}}$$

2.4.3 Sample entropy (SampEn) of CoG

The sample entropy was used to assess the regularity or predictability within CoG movements in time-series collected under different conditions and in different experimental groups (e.g., genders). The working definition in studies (Richman and Mooram, 2000; Lubetzky et al., 2018; Montesinos et al., 2018; Lin et al., 2022) was that more regular movements represented more predictable movements, required less degree of freedom of movements, and produced lower entropy values. In contrast, more irregular movements indicated less predictable movements, required higher degrees of freedom of movements, and produced higher entropy values. SampEn was calculated by the negative natural logarithm of the conditional probabilities that a series of data pointed a certain distance apart, m , would repeat itself at $m+1$. Also, SampEn took the logarithm of the sum of conditional probabilities as SampEn (m, γ, τ, N), where m was the embedding dimension, γ was tolerance, τ was the time delay, and N was a time-series data set of length.

$$\text{SampEn} = -\ln \frac{d[X_{m+1}(i), X_{m+1}(j)]}{d[X_m(i), X_m(j)]}$$

where both $d[x_m(i), x_m(j)]$ and $d[x_{m+1}(i), x_{m+1}(j)]$ were smaller than γ . The $\gamma = 0.2$ and $m = 3$ were set in this study, followed by Montesinos et al. (2018). In Montesinos et al.'s study, applying $\gamma = 0.2$ and $m = 3$ can identify the subtle differences in center of pressure trajectories between the older fallers and older non-fallers. This

present study also followed Lin et al., 2022 that applying time delay ($\tau = 5$) to the CoG data in both AP and ML directions. After an adjustment from 100 Hz to 20 Hz using time delay ($\tau = 5$), a length of N became a data set of 1,800 data points (20 Hz \times 90 s; Lin et al., 2022; Montesinos et al., 2018). The rationale using time delay was that using a unity delay ($\tau = 1$) might only catch the linear autocorrelation properties of the signal and would mask the ability of SampEn to quantify the “true” regularity and non-linear feature in the time-series (Kaffashi et al., 2008).

2.5 Statistical analysis

A Shapiro-Wilk normality test with an alpha value of 0.05 was used to evaluate the normality for each dependent variable. The dependent variables were total traveling distance of CoG, PR of CoG and SampEn of CoG values in both AP and ML directions. Also, an independent t-test was used to compare the weight and height between females and males.

- If the data were normally distributed, a three-way mixed repeated measure ANOVA (2 SOT conditions \times 3 VS \times 2 sex groups) was applied to investigate the VS effect, the sex effect, VS effect as well as the interaction between these three effects. Post-hoc comparisons using the Tukey method were performed if an interaction existed in each dependent variable.
- If the data was not normally distributed, the Brunner and Langer non-parametric longitudinal data model was used to investigate the within-participant effect (2 SOT conditions \times 3 VS conditions) and the between-participants effect (2 sex groups) (Brunner et al., 2002). The Wilcoxon Signed Rank Test was used for *post hoc* comparisons comparing the effects of different SOT conditions in each group if there existed an interaction. Comparing sex groups in each SOT condition with/without different VS were conducted using the Mann-Whitney U-test.

The sample size of this study was based on the previous study's result (Chiu and Wang, 2007), recruitment of 15 males and 15 females would generate a power of 80% and a level of significance of 5% (two-sided) for detecting a true difference in muscle activation between the males and females during walking. The partial eta squared method was used to evaluate effect size in the present study, based on Cohen's guideline 0.138 for a large effect size, 0.059 for a moderate effect size, and 0.01 for a small effect size (Cohen, 1988). Statistical analysis was completed in SPSS 26.0 (IBM Corporation, Armond, NY).

3 Results

3.1 Participant's information

In this study, there was no statistical sex differences in age (females: 35.06 \pm 17.83 years old vs. males: 34.80 \pm 17.50 years old) but in weight (females: 60.93 \pm 9.31 kg vs. 75.4 \pm 10.29 kg, $p < 0.001$) and in height (females: 165.60 \pm 5.09 kg vs. 174.80 \pm 6.00 kg, $p < 0.001$).

3.2 Normality tests

The results of the Shapiro-Wilk test revealed that the alpha value was greater than 0.05 for total traveling distances, PR values, SampEn values in both AP and ML directions, indicating the normal distribution. Thus, a three-way mixed ANOVA (2 SOT conditions \times 3 VS \times 2 sex groups) was applied to investigate the VS effect, the sex effect, VS effect as well as the interaction between these three effects.

3.3 The results of mixed three-way repeated measure

3.3.1 The effect of sex

A significant effect of sex was found in the PR in the AP direction ($F_{1, 28} = 5.548$, $p = 0.026$), in the SampEn values in the AP directions ($F_{1, 28} = 5.611$, $p = 0.025$) and in the ML direction ($F_{1, 28} = 92.164$, $p < 0.001$). The results showed that females demonstrated greater PR value in the AP direction than in males. Also, significantly greater Entropy values were found in both AP and ML directions. More details are shown in Tables 1–6.

3.3.2 The interaction between the effect of sex and the effect of different SOT conditions

A significant interaction was found in the total traveling distance in the AP direction ($F_{1, 28} = 5.735$, $p = 0.024$), in the PR in the AP direction ($F_{1, 28} = 5.876$, $p = 0.022$), in the PR in the ML direction ($F_{1, 28} = 6.712$, $p = 0.015$), in the SampEn values in the AP directions ($F_{1, 28} = 11.749$, $p = 0.002$) and in the ML direction ($F_{2, 56} = 52.621$, $p < 0.001$). More details are shown in Tables 1–6.

3.3.3 The interaction between the effect of sex and the effect of VS

A significant interaction was found in the total traveling distance in the AP direction ($F_{2, 56} = 3.975$, $p = 0.024$), in the PR in the ML direction ($F_{2, 56} = 9.308$, $p < 0.001$), in the SampEn values in the AP directions ($F_{2, 56} = 4.781$, $p = 0.012$) and in the ML direction ($F_{2, 56} = 20.572$, $p < 0.001$). More details are shown in Tables 1–6.

3.3.4 The interaction among the effect of sex, the effect of SOT condition, and the effect of VS

A significant interaction was found in total traveling distance in the AP direction ($F_{2, 56} = 3.379$, $p = 0.041$), in the PR in the ML direction ($F_{2, 56} = 16.809$, $p < 0.001$), in the SampEn values in the AP directions ($F_{2, 56} = 7.118$, $p = 0.002$) and in the ML direction ($F_{2, 56} = 50.889$, $p < 0.001$). Pairwise comparisons corrected by Tukey method revealed that the total traveling distance in the AP direction was significantly less in females than in males ($p = 0.01$, Figure 2), and the PR in the ML direction was significantly greater in females than in males while standing ($p = 0.001$, Figure 3) in SOT5 with Bi VS. Also, For the Entropy measure, significantly greater SampEn values were found in females than in males in the AP ($p < 0.001$) and in the ML ($p < 0.001$) directions while standing in SOT1 with Bi VS. More details were shown in Figure 4.

TABLE 1 The statistical results of Performance ratio of Center of Gravity in the anterior-posterior direction (PR_AP). SOT1, sensory organization test condition 1; SOT5, sensory organization test condition 5; VS, vestibular stimulation; N, no VS, Uni, unilateral VS; Bi, bilateral VS; Female-SOT1, females stood in SOT1; Female-SOT5, females stood in SOT5; Male-SOT1, males stood in SOT1; Male-SOT5, males stood in SOT5; Female-N, female stood without VS; Female-Uni, females stood with unilateral VS; Female-Bi, females stood with bilateral VS; Male-N, males stood without VS; Male-Uni, males stood with unilateral VS; Male-Bi, males stood with bilateral VS; SOT1-N, standing in SOT1 without VS; SOT1-Uni, standing in SOT1 with unilateral VS; SOT1-Bi, standing in SOT1 with bilateral VS; SOT5-N, standing in SOT5 without VS; SOT5-Uni, standing in SOT5 with unilateral VS; SOT5-Bi, standing in SOT5 with bilateral VS; NA, the interaction did not reach the significant level; NS, not significant.

PR_AP (%)		Means (Std)	Sex	SOT Conditions	VS	Sex x SOT Conditions	Sex x VS	VS x SOT Conditions	Sex x SOT Conditions x VS					
SOT1-N	Female	13.432 (3.128)	$p = 0.026$	$p < 0.001$	$p < 0.001$	$p = 0.022$	$p = 0.247$	$p < 0.001$	$p = 0.059$					
	Male	13.350 (4.884)												
SOT1-Uni	Female	19.228 (5.792)	Sex x SOT Conditions	Female-SOT1	Male-SOT1	Female-SOT5	Male-SOT5	Sex x VS	Female-N	Female-Uni	Female-Bi	Male-N	Male-Uni	Male-Bi
	Male	17.594 (5.726)	Female-SOT1		NS	$p < 0.001$	$p < 0.001$	Female-N		NA	NA	NA	NA	NA
SOT1-Bi	Female	22.235 (6.293)	Male-SOT1	NS		$p < 0.001$	$p < 0.001$	Female-Uni	NA		NA	NA	NA	NA
	Male	20.808 (7.292)	Female-SOT5	$p < 0.001$	$p < 0.001$		$p < 0.001$	Female-Bi	NA	NA		NA	NA	NA
SOT5-N	Female	59.082 (23.543)	Male-SOT5	$p < 0.001$	$p < 0.001$	$p < 0.001$		Male-N	NA	NA	NA		NA	NA
	Male	40.425 (8.506)						Male-Uni	NA	NA	NA	NA		NA
SOT5-Uni	Female	64.323 (21.737)	Sex	Female vs. Male				Male-Bi	NA	NA	NA	NA	NA	
	Male	50.228 (11.709)		$p = 0.026$				VS x SOT Conditions	SOT1-N	SOT1-Uni	SOT1-Bi	SOT5-N	SOT5-Uni	SOT5-Bi
SOT5-Bi	Female	73.805 (18.324)	SOT Conditions	SOT1 vs. SOT5				SOT1-N		NS	NS	$p < 0.001$	$p < 0.001$	$p < 0.001$
	Male	61.789 (12.749)		$p < 0.001$				SOT1-Uni	NS		NS	$p < 0.001$	$p < 0.001$	$p < 0.001$
			VS	N vs. Uni	N vs. Bi	Uni Vs. Bi		SOT1-Bi	NS	NS		$p < 0.001$	$p < 0.001$	$p < 0.001$
				$p < 0.001$	$p < 0.001$	$p < 0.001$		SOT5-N	$p < 0.001$	$p < 0.001$	$p < 0.001$		NS	$p < 0.001$
								SOT5-Uni	$p < 0.001$	$p < 0.001$	$p < 0.001$	NS		$p = 0.037$
								SOT5-Bi	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.037$	

TABLE 2 The statistical results of Performance ratio of Center of Gravity in the medial-lateral direction (PR_ML). SOT1, sensory organization test condition 1; SOT5, sensory organization test condition 5; VS, vestibular stimulation; N, no VS; Uni, unilateral VS; Bi, bilateral VS; Female-SOT1, females stood in SOT1; Female-SOT5, females stood in SOT5; Male-SOT1, males stood in SOT1; Male-SOT5, males stood in SOT5; Female-N, female stood without VS; Female-Uni, females stood with unilateral VS; Female-Bi, females stood with bilateral VS; Male-N, males stood without VS; Male-Uni, males stood with unilateral VS; Male-Bi, males stood with bilateral VS; SOT1-N, standing in SOT1 without VS; SOT1-Uni, standing in SOT1 with unilateral VS; SOT1-Bi, standing in SOT1 with bilateral VS; SOT5-N, standing in SOT5 without VS; SOT5-Uni, standing in SOT5 with unilateral VS; SOT5-Bi, standing in SOT5 with bilateral VS; NA, the interaction did not reach the significant level; NS, not significant.

PR_ML (%)		Means (Std)	Sex	SOT conditions	VS	Sex x SOT conditions	Sex x VS	VS x SOT conditions	Sex x SOT conditions x VS					
SOT1-N	Female	13.578 (2.987)	$p = 0.263$	$p < 0.001$	$p < 0.001$	$p = 0.015$	$p < 0.001$	$p = 0.003$	$p < 0.001$					
	Male	14.836 (5.267)												
SOT1-Uni	Female	26.118 (9.505)	Sex x SOT Conditions	Female-SOT1	Male-SOT1	Female-SOT5	Male-SOT5	Sex x VS	Female-N	Female-Uni	Female-Bi	Male-N	Male-Uni	Male-Bi
	Male	25.882 (8.983)	Female-SOT1		NS	$p < 0.001$	$p < 0.001$	Female-N		$p = 0.028$	$p = 0.009$	NS	$p = 0.009$	NS
SOT1-Bi	Female	19.731 (8.163)	Male-SOT1	NS		$p < 0.001$	$p < 0.001$	Female-Uni	$p = 0.028$		NS	$p = 0.001$	NS	NS
	Male	20.754 (7.181)	Female-SOT5	$p < 0.001$	$p < 0.001$		$p = 0.018$	Female-Bi	$p = 0.009$	NS		$p < 0.001$	NS	NS
SOT5-N	Female	30.967 (7.705)	Male-SOT5	$p < 0.001$	$p < 0.001$	$p = 0.018$		Male-N	NS	$p = 0.001$	$p < 0.001$		$p < 0.001$	NS
	Male	23.591 (7.076)						Male-Uni	$p = 0.009$	NS	NS	$p < 0.001$		NS
SOT5-Uni	Female	39.282 (12.732)	Sex	Female vs. Male				Male-Bi	NS	NS	NS	NS	NS	
	Male	42.014 (15.693)		$p = 0.263$				VS x SOT Conditions	SOT1-N	SOT1-Uni	SOT1-Bi	SOT5-N	SOT5-Uni	SOT5-Bi
SOT5-Bi	Female	48.182 (15.872)	SOT Conditions	SOT1 vs. SOT5				SOT1-N		$p < 0.001$	NS	$p < 0.001$	$p < 0.001$	$p < 0.001$
	Male	30.939 (10.685)		$p < 0.001$				SOT1-Uni	$p < 0.001$		NS	NS	$p < 0.001$	$p < 0.001$
			VS	N vs. Uni	N vs. Bi	Uni Vs. Bi		SOT1-Bi	NS	NS		NS	$p < 0.001$	$p < 0.001$
				$p < 0.001$	$p < 0.001$	$p = 0.011$		SOT5-N	$p < 0.001$	NS	NS		$p < 0.001$	$p < 0.001$
								SOT5-Uni	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$		NS
								SOT5-Bi	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$	NS	

TABLE 3 The statistical results of Sample Entropy of Center of Gravity in the anterior-posterior direction (SampEn_AP). SOT1, sensory organization test condition 1; SOT5, sensory organization test condition 5; VS, vestibular stimulation; N, no VS; Uni, unilateral VS; Bi, bilateral VS; Female-SOT1, females stood in SOT1; Female-SOT5, females stood in SOT5; Male-SOT1, males stood in SOT1; Male-SOT5, males stood in SOT5; Female-N, female stood without VS; Female-Uni, females stood with unilateral VS; Female-Bi, females stood with bilateral VS; Male-N, males stood without VS; Male-Uni, males stood with unilateral VS; Male-Bi, males stood with bilateral VS; SOT1-N, standing in SOT1 without VS; SOT1-Uni, standing in SOT1 with unilateral VS; SOT1-Bi, standing in SOT1 with bilateral VS; SOT5-N, standing in SOT5 without VS; SOT5-Uni, standing in SOT5 with unilateral VS; SOT5-Bi, standing in SOT5 with bilateral VS; NA, the interaction did not reach the significant level; NS, not significant.

SampEn_AP		Means(Std)	Sex	SOT conditions	VS	Sex x SOT conditions	Sex x VS	VS x SOT conditions	Sex x SOT conditions x VS					
SOT1-N	Female	0.134 (0.040)	$p = 0.025$	$p < 0.001$	$p < 0.001$	$p = 0.002$	$p = 0.012$	$p < 0.001$	$p = 0.002$					
	Male	0.108 (0.036)												
SOT1-Uni	Female	0.164 (0.056)	Sex x SOT Conditions	Female-SOT1	Male-SOT1	Female-SOT5	Male-SOT5	Sex x VS	Female-N	Female-Uni	Female-Bi	Male-N	Male-Uni	Male-Bi
	Male	0.126 (0.033)	Female-SOT1		$p < 0.001$	$p < 0.001$	$p < 0.001$	Female-N		NS	NS	NS	NS	NS
SOT1-Bi	Female	0.207 (0.059)	Male-SOT1	$p < 0.001$		$p < 0.001$	$p < 0.001$	Female-Uni	NS		NS	NS	NS	NS
	Male	0.138 (0.037)	Female-SOT5	$p < 0.001$	$p < 0.001$		NS	Female-Bi	NS	NS		NS	NS	NS
SOT5-N	Female	0.074 (0.019)	Male-SOT5	$p < 0.001$	$p < 0.001$	NS		Male-N	NS	NS	NS		NS	NS
	Male	0.074 (0.022)						Male-Uni	NS	NS	NS	NS		NS
SOT5-Uni	Female	0.061 (0.019)	Sex	Female vs. Male				Male-Bi	NS	NS	NS	NS	NS	
	Male	0.063 (0.019)		$p = 0.025$				VS x SOT Conditions	SOT1-N	SOT1-Uni	SOT1-Bi	SOT5-N	SOT5-Uni	SOT5-Bi
SOT5-Bi	Female	0.051 (0.015)	SOT Conditions	SOT1 vs. SOT5				SOT1-N		NS	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
	Male	0.055 (0.018)		$p < 0.001$				SOT1-Uni	NS		NS	$p < 0.001$	$p < 0.001$	$p < 0.001$
			VS	N vs. Uni	N vs. Bi	Uni Vs. Bi		SOT1-Bi	$p < 0.001$	NS		$p < 0.001$	$p < 0.001$	$p < 0.001$
				$p = 0.091$	$p = 0.023$	$p = 0.021$		SOT5-N	$p < 0.001$	$p < 0.001$	$p < 0.001$		NS	NS
								SOT5-Uni	$p < 0.001$	$p < 0.001$	$p < 0.001$	NS		NS
								SOT5-Bi	$p < 0.001$	$p < 0.001$	$p < 0.001$	NS	NS	

TABLE 4 The statistical results of Sample Entropy of Center of Gravity in the medial-lateral direction (SampEn_ML). SOT1, sensory organization test condition 1; SOT5, sensory organization test condition 5; VS, vestibular stimulation; N, no VS; Uni, unilateral VS; Bi, bilateral VS; Female-SOT1, females stood in SOT1; Female-SOT5, females stood in SOT5; Male-SOT1, males stood in SOT1; Male-SOT5, males stood in SOT5; Female-N, female stood without VS; Female-Uni, females stood with unilateral VS; Female-Bi, females stood with bilateral VS; Male-N, males stood without VS; Male-Uni, males stood with unilateral VS; Male-Bi, males stood with bilateral VS; SOT1-N, standing in SOT1 without VS; SOT1-Uni, standing in SOT1 with unilateral VS; SOT1-Bi, standing in SOT1 with bilateral VS; SOT5-N, standing in SOT5 without VS; SOT5-Uni, standing in SOT5 with unilateral VS; SOT5-Bi, standing in SOT5 with bilateral VS; NA, the interaction did not reach the significant level; NS, not significant.

SampEn_ML		Means (Std)	Sex	SOT conditions	VS	Sex x SOT conditions	Sex x VS	VS x SOT conditions	Sex x SOT conditions x VS					
SOT1-N	Female	0.175 (0.049)	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$					
	Male	0.071 (0.023)												
SOT1-Uni	Female	0.349 (0.099)	Sex x SOT Conditions	Female-SOT1	Male-SOT1	Female-SOT5	Male-SOT5	Sex x VS	Female-N	Female-Uni	Female-Bi	Male-N	Male-Uni	Male-Bi
	Male	0.092 (0.028)	Female-SOT1		$p < 0.001$	$p < 0.001$	$p < 0.001$	Female-N		$p = 0.001$	NS	$p < 0.001$	$p = 0.001$	$p = 0.001$
SOT1-Bi	Female	0.247 (0.059)	Male-SOT1	$p < 0.001$		$p = 0.001$	NS	Female-Uni	$p = 0.001$		$p = 0.003$	$p < 0.001$	$p < 0.001$	$p < 0.001$
	Male	0.116 (0.047)	Female-SOT5	$p < 0.001$	$p = 0.001$		$p < 0.001$	Female-Bi	NS	$p = 0.003$		$p < 0.001$	$p < 0.001$	$p < 0.001$
SOT5-N	Female	0.174 (0.034)	Male-SOT5	$p < 0.001$	NS	$p < 0.001$		Male-N	$p < 0.001$	$p < 0.001$	$p < 0.001$		NS	NS
	Male	0.069 (0.018)						Male-Uni	$p = 0.001$	$p < 0.001$	$p < 0.001$	NS		NS
SOT5-Uni	Female	0.142 (0.031)	Sex	Female vs. Male				Male-Bi	$p = 0.001$	$p < 0.001$	$p < 0.001$	NS	NS	
	Male	0.114 (0.031)		$p < 0.001$				VS x SOT Conditions	SOT1-N	SOT1-Uni	SOT1-Bi	SOT5-N	SOT5-Uni	SOT5-Bi
SOT5-Bi	Female	0.112 (0.029)	SOT Conditions	SOT1 vs. SOT5				SOT1-N		$p < 0.001$	NS	NS	NS	NS
	Male	0.088 (0.018)		$p < 0.001$				SOT1-Uni	$p < 0.001$		NS	$p < 0.001$	$p < 0.001$	$p < 0.001$
			VS	N vs. Uni	N vs. Bi	Uni Vs. Bi		SOT1-Bi	NS	NS		NS	NS	$p = 0.002$
				$p < 0.001$	$p < 0.001$	$p = 0.022$		SOT5-N	NS	$p < 0.001$	NS		NS	NS
								SOT5-Uni	NS	$p < 0.001$	NS	NS		NS
								SOT5-Bi	NS	$p < 0.001$	$p = 0.002$	NS	NS	

TABLE 5 The statistical results of Traveling distance of Center of Gravity in the anterior-posterior direction (TD in AP). SOT1, sensory organization test condition 1; SOT5, sensory organization test condition 5; VS, vestibular stimulation; N, no VS, Uni, unilateral VS; Bi, bilateral VS; Female-SOT1, females stood in SOT1; Female-SOT5, females stood in SOT5; Male-SOT1, males stood in SOT1; Male-SOT5, males stood in SOT5; Female-N, female stood without VS; Female-Uni, females stood with unilateral VS; Female-Bi, females stood with bilateral VS; Male-N, males stood without VS; Male-Uni, males stood with unilateral VS; Male-Bi, males stood with bilateral VS; SOT1-N, standing in SOT1 without VS; SOT1-Uni, standing in SOT1 with unilateral VS; SOT1-Bi, standing in SOT1 with bilateral VS; SOT5-N, standing in SOT5 without VS; SOT5-Uni, standing in SOT5 with unilateral VS; SOT5-Bi, standing in SOT5 with bilateral VS; NS, not significant.

TD in AP (m)		Means (Std)	Sex	SOT conditions	VS	Sex x SOT conditions	Sex x VS	VS x SOT conditions	Sex x SOT conditions x VS					
SOT1-N	Female	1.396 (0.235)	$p = 0.158$	$p < 0.001$	$p < 0.001$	$p = 0.024$	$p = 0.024$	$p < 0.001$	$p = 0.041$					
	Male	1.203 (0.141)												
SOT1-Uni	Female	1.468 (0.232)	Sex x SOT Conditions	Female-SOT1	Male-SOT1	Female-SOT5	Male-SOT5	Sex x VS	Female-N	Female-Uni	Female-Bi	Male-N	Male-Uni	Male-Bi
	Male	1.321 (0.167)	Female-SOT1		NS	$p < 0.001$	$p < 0.001$	Female-N		NS	NS	NS	NS	$p = 0.018$
SOT1-Bi	Female	1.567 (0.324)	Male-SOT1	$p = 0.855$		$p < 0.001$	$p < 0.001$	Female-Uni	NS		NS	NS	NS	NS
	Male	1.404 (0.189)	Female-SOT5	$p < 0.001$	$p < 0.001$		$p = 0.001$	Female-Bi	NS	NS		NS	NS	NS
SOT5-N	Female	2.597 (0.521)	Male-SOT5	$p < 0.001$	$p < 0.001$	$p = 0.001$		Male-N	NS	NS	NS		NS	$p = 0.036$
	Male	2.977 (1.113)						Male-Uni	NS	NS	NS	NS		NS
SOT5-Uni	Female	3.136 (0.729)	Sex	Female vs. Male				Male-Bi	$p = 0.018$	NS	NS	$p = 0.036$	NS	
	Male	3.924 (1.596)		$p = 0.158$				VS x Conditions	SOT1-N	SOT1-Uni	SOT1-Bi	SOT5-N	SOT5-Uni	SOT5-Bi
SOT5-Bi	Female	3.814 (1.038)	SOT Conditions	SOT1 vs. SOT5				SOT1-N		NS	NS	$p < 0.001$	$p < 0.001$	$p < 0.001$
	Male	5.051 (1.863)		$p < 0.001$				SOT1-Uni	NS		NS	$p < 0.001$	$p < 0.001$	$p < 0.001$
			VS	N vs. Uni	N vs. Bi	Uni Vs. Bi		SOT1-Bi	NS	NS		$p < 0.001$	$p < 0.001$	$p < 0.001$
				$p < 0.001$	$p < 0.001$	$p < 0.001$		SOT5-N	$p < 0.001$	$p < 0.001$	$p < 0.001$		$p = 0.027$	$p < 0.001$
								SOT5-Uni	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.027$		$p = 0.003$
								SOT5-Bi	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.003$	

TABLE 6 The statistical results of Traveling distance of Center of Gravity in the medial-lateral direction (TD in ML). SOT1, sensory organization test condition 1, SOT5, sensory organization test condition 5; VS, vestibular stimulation; N, no VS; Uni, unilateral VS; Bi, bilateral VS; Female-SOT1, females stood in SOT1; Female-SOT5, females stood in SOT5; Male-SOT1, males stood in SOT1; Male-SOT5, males stood in SOT5; Female-N, female stood without VS; Female-Uni, females stood with unilateral VS; Female-Bi, females stood with bilateral VS; Male-N, males stood without VS; Male-Uni, males stood with unilateral VS; Male-Bi, males stood with bilateral VS; SOT1-N, standing in SOT1 without VS; SOT1-Uni, standing in SOT1 with unilateral VS; SOT1-Bi, standing in SOT1 with bilateral VS; SOT5-N, standing in SOT5 without VS; SOT5-Uni, standing in SOT5 with unilateral VS; SOT5-Bi, standing in SOT5 with bilateral VS; NA: the interaction did not reach the significant level; NS, not significant.

TD in ML (m)		Means (Std)	Sex	Conditions	VS	Sex x conditions	Sex x VS	VS x conditions	Sex x conditions x VS					
SOT1-N	Female	1.005 (0.157)	$p = 0.251$	$p < 0.001$	$p < 0.001$	$p = 0.137$	$p = 0.384$	$p = 0.016$	$p = 0.802$					
	Male	0.829 (0.109)												
SOT1-Uni	Female	1.034 (0.178)	Sex x Conditions	Female-SOT1	Male-SOT1	Female-SOT5	Male-SOT5	Sex x VS	Female-N	Female-Uni	Female-Bi	Male-N	Male-Uni	Male-Bi
	Male	0.919 (0.191)	Female-SOT1		NA	NA	NA	Female-N		NA	NA	NA	NA	NA
SOT1-Bi	Female	1.056 (0.186)	Male-SOT1	NA		NA	NA	Female-Uni	NA		NA	NA	NA	NA
	Male	0.966 (0.216)	Female-SOT5	NA	NA		NA	Female-Bi	NA	NA		NA	NA	NA
SOT5-N	Female	1.186 (0.219)	Male-SOT5	NA	NA	NA		Male-N	NA	NA	NA		NA	NA
	Male	1.135 (0.293)						Male-Uni	NA	NA	NA	NA		NA
SOT5-Uni	Female	1.375 (0.262)	Sex	Female vs. Male				Male-Bi	NA	NA	NA	NA	NA	
	Male	1.371 (0.209)		NS				VS x Conditions	SOT1-N	SOT1-Uni	SOT1-Bi	SOT5-N	SOT5-Uni	SOT5-Bi
SOT5-Bi	Female	1.346 (0.329)	Conditions	SOT1 vs. SOT5				SOT1-N		NS	NS	$p = 0.001$	$p < 0.001$	$p < 0.001$
	Male	1.314 (0.291)		$p < 0.001$				SOT1-Uni	NS		NS	$p = 0.026$	$p < 0.001$	$p < 0.001$
			VS	N vs. Uni	N vs. Bi	Uni Vs. Bi		SOT1-Bi	NS	NS		NS	$p < 0.001$	$p < 0.001$
				$p < 0.001$	$p < 0.001$	NS		SOT5-N	$p = 0.001$	$p = 0.026$	NS		$p = 0.006$	$p = 0.054$
								SOT5-Uni	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.006$		NS
								SOT5-Bi	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.054$	NS	

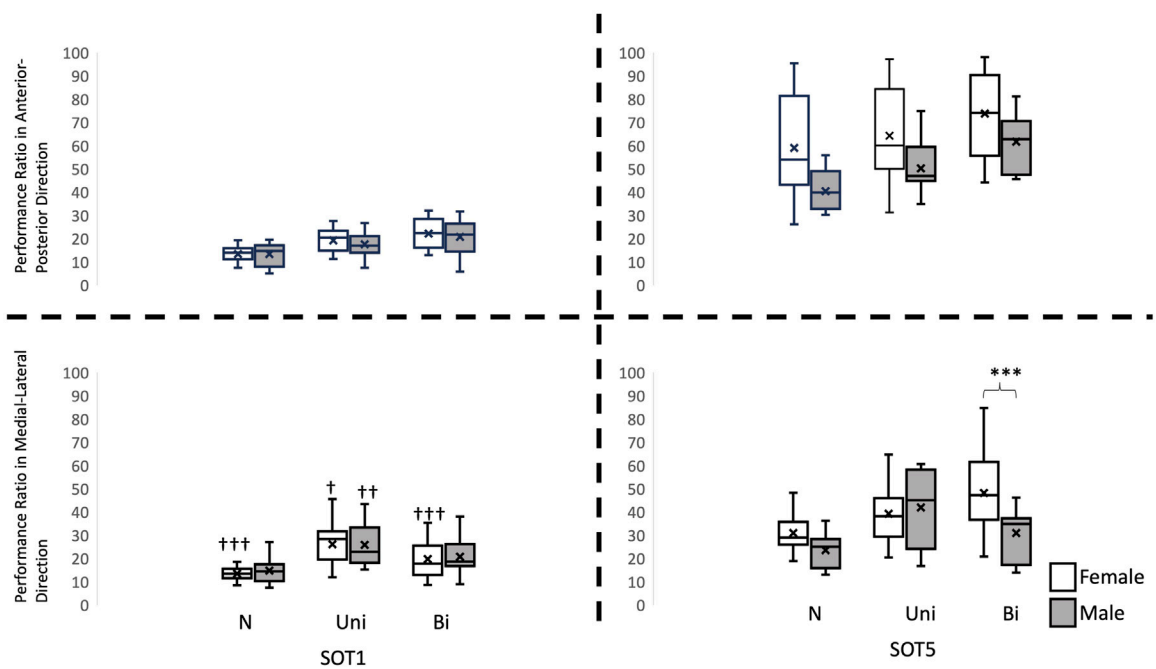


FIGURE 2 Performance ratio of Center of Gravity in the anterior-posterior and medial-lateral direction. †: indicates a significant difference between Sensory organization test condition 1 (SOT 1) and condition 5 (SOT 5). *: indicates a significant difference between genders. N: no vestibular stimulation. Uni: unilateral vestibular stimulation. Bi: bilateral vestibular stimulation.

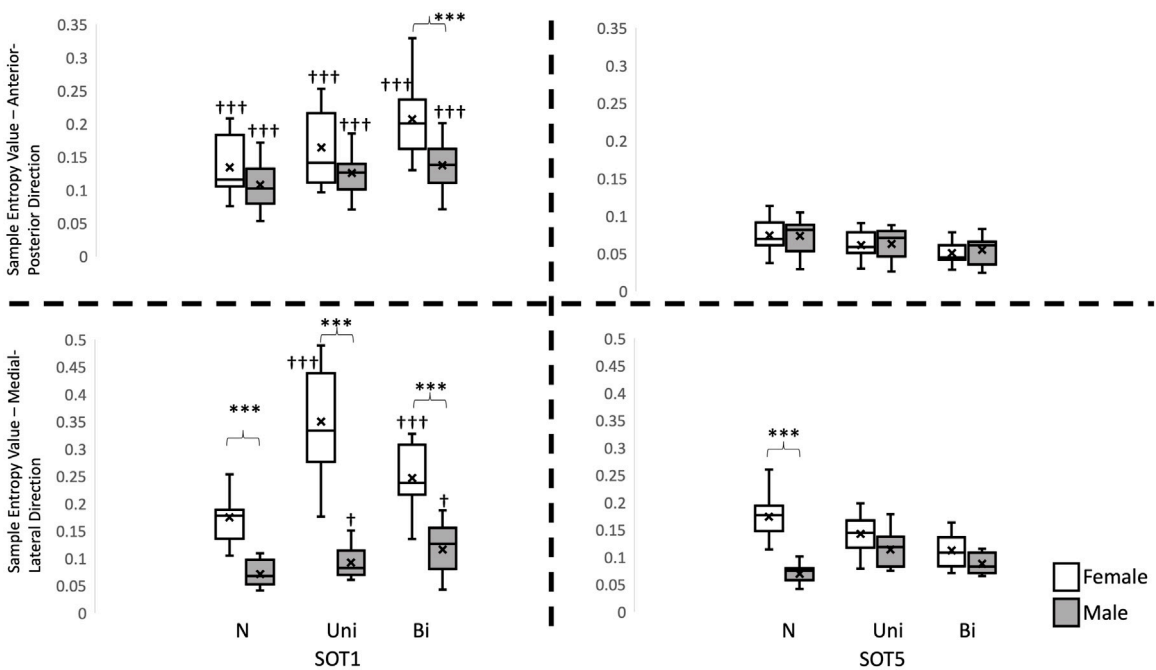


FIGURE 3 Sample Entropy values of Center of Gravity in the anterior-posterior and medial-lateral direction. †: indicates a significant difference between Sensory organization test condition 1 (SOT 1) and condition 5 (SOT 5). *: indicates a significant difference between genders. N: no vestibular stimulation. Uni: unilateral vestibular stimulation. Bi: bilateral vestibular stimulation.

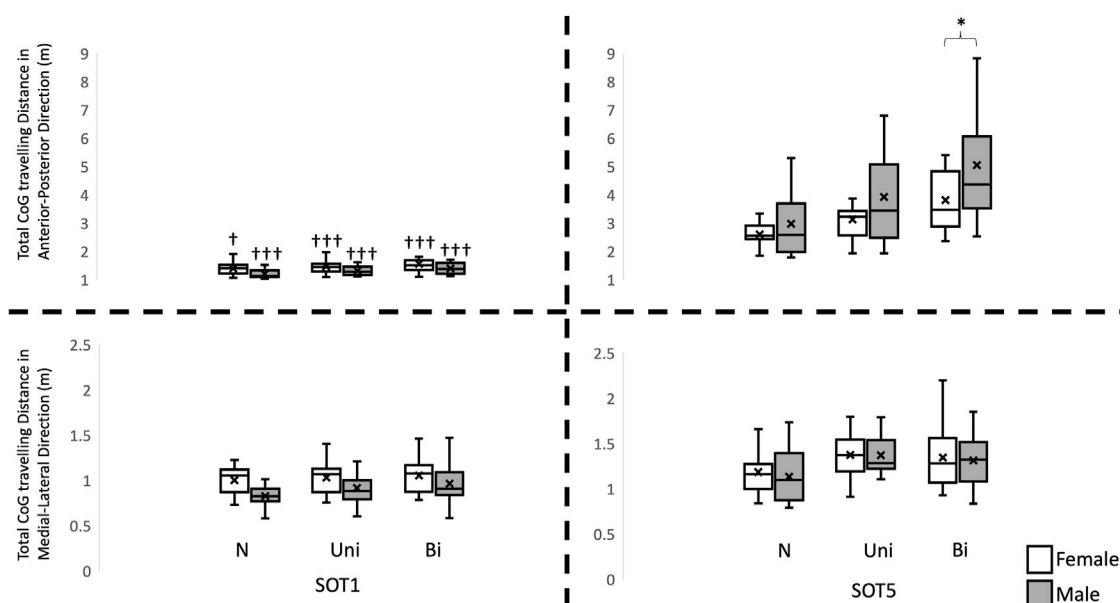


FIGURE 4

Total Center of gravity travelling distance in the anterior-posterior and medial-lateral direction. †: indicates a significant difference between Sensory organization test condition 1 (SOT 1) and condition 5 (SOT 5). *: indicates a significant difference between genders. N: no vestibular stimulation. Uni: unilateral vestibular stimulation. Bi: bilateral vestibular stimulation.

4 Discussions

It was the objective of this study to determine whether or not sex effect impacted balance control with/without VS during standing in normal and vestibular-demanding situations. Results mostly confirmed the hypothesis that 1) females demonstrated greater PR of CoG in the AP direction and SampEn of CoG in both AP and ML directions than males regardless of whether VS was administered or what SOT conditions participants were in, 2) All participants, regardless of whether VS was administered, showed an increase in PR of CoG, but a decrease in SampEn of CoG, when standing in SOT5 compared to standing in SOT1. Furthermore, females showed greater increases in PR and decreased SampEn of CoG than males in SOT5, 3) Regardless of the SOT conditions participants stood in, VS had a greater impact on females than on males, and 4) As compared to other conditions, females showed the greatest PR of CoG when standing in vestibular-demanding and bilaterally vestibular-disturbed conditions (SOT5, the most challenging task).

4.1 A sex effect on balance control

This study was funded by NASA in order to determine whether there were any differences in balance control between the sexes when performing a simple task - standing. Regardless of whether VS was administered or what SOT conditions participants were in, healthy females had a greater PR of CoG in the AP direction and a greater SampEn of CoG in both directions than healthy males. In contrast to males, females controlled balance by largely adjusting instantaneous sway, as evidenced by a greater PR of CoG. Moreover, a greater SampEn of CoG may be explained by the fact that females used

higher degrees of freedom in their movement patterns (more irregular movements) as a result of an exploratory approach to maintain balance in both the AP and ML directions in time series (Chien et al., 2016). The above-mentioned differences in balance control between men and women may be the result of physiological and anatomical differences (Bowman et al., 2000; Corazzi et al., 2020; Lien and Yang, 2021; El Khiati et al., 2022), as well as differences in body mass and height (Greve et al., 2013). In light of these findings, it is apparent that both rehabilitation for patients with vestibular disorders and the diagnosis of astronauts' sensorimotor functions should consider sex effects on balance control. It was also noted that the balance control could be improved by utilizing a real-time visual feedback system of CoG trajectory (Wang et al., 2021). Specifically, this type of training has been shown to improve balance control more in females than in males (Wang et al., 2021).

4.2 The interaction between the sex effect and SOT condition effect

As expected, both sexes showed a greater PR of CoG when standing under vestibular-demanding conditions (SOT5) than when standing normally (SOT1). Also, whether or not VS was applied, the sex effect on PR of CoG in both AP and ML directions as well as SampEn of CoG in ML directions was significant while standing SOT5. These results could be explained by the concept of internal model (Merfeld et al., 1999). The term internal model referred to the notion that the central nervous system (CNS) was capable of storing and updating information about the body in light of its external environment. To illustrate, in this study, a participant with blindfolded while standing on a sway-reference

support surface (SOT5) could generate an initial internal model (self-estimate) based on previous life experiences. As the surface began to rotate with respect to this participant, the initial internal model might become inaccurate. This might result in CNS having to prepare for another revision, thereby causing an increase in PR of CoG and an decrease in SampEn of CoG. It was possible that the PR of CoG of this participant might decrease gradually after becoming familiar with the scenario. Based on the abovementioned procedures, Ito (2008) proposed a conceptual structure of an internal model that control contained several major components: an instructor (prefrontal cortex), controller (motor cortex), controlled object (a body part), sensory system (visual, somatosensory, vestibular systems), forward model, and inverse model. In the current study, while standing in SOT5, the instructor (prefrontal cortex) first received environmental information from sensory systems (mostly from the vestibular system since two other sensory systems were disrupted) and then instructed the controller (motor cortex) accordingly. As a next step, the controller sent a motor command to a body part in order to maintain balance. Also, the controller sent a signal back to the internal model (forward model) to compare the actual body position with the predicted body position. When the predicted body position differs from the actual body position, the forward model may correct the differences and send the correction back to the motor cortex. As a result of repeatedly executing the procedure described above, the internal model was well-trained and turned to an inverse model for handling the similar situation rapidly next time, presenting better balance control in the same SOT 5 (Wolfson et al., 1994). As a result of this concept, it was reasonable to assume that the different anatomical structures within the vestibular system between males and females (Bowman et al., 2000; Corazzi et al., 2020; Lien and Yang, 2021; El Khiati et al., 2022) resulted in instructors (prefrontal cortex) giving different instructions to controllers (motor cortex) when the vestibular system was heavily relied. This resulted in a increase in PR of CoG and SampEn of CoG for females than males (when standing in SOT5). Despite the absence of sensorimotor training in this study, the above-mentioned procedure can serve as the basis for sensorimotor training in pathological groups, such as patients with vestibular disorders and astronauts. It was possible to develop an appropriate internal model for dealing with unfamiliar and unpredictable situations, such as those encountered on the moon and on Mars, by continuously exploring unfamiliar sensory-conflicted environment.

Standing in different sensory-conflicted situations, the PR of CoG would represent the outcomes of balance control, while the SampEn of CoG would represent the pathways to achieve these outcomes. One well-known example was Bernstein's hammer stroke experiment (1923). A simple hammer stroke task could be extremely complex in Bernstein's study (1923), and nails could be hit in a variety of ways, including abductive and vertical strokes. Despite similar trajectories, there were differences in the changes in joint coordinates or muscle activation over time in hammerheads. According to the findings of the present study, both males and females utilized lower degrees of freedom in balance control (less random) in SOT5 than in SOT1 in the AP direction. Furthermore, only females, but not males, exhibited a lower degree of freedom in balance control in the ML direction in

SOT5 compared to SOT1. These decreases in degrees of freedom in males and females could be explained as the first response to handle unfamiliar situation. In the current study, none of these participants experienced standing in SOT5 environment; therefore, to limit the degree of freedom in the movement might be the most convenient method to maintain the balance control (Lin et al., 2022) while standing with blindfolded and sway-reference surface. It has been reported that females tended to rely on somatosensory system more than males to control balance while standing on moving surface (Schulleri et al., 2022). Thus, in SOT5, females reduced degrees of freedom not only in the AP direction, but also in the ML direction. This may be due to females having difficulties dealing with balance control while both visual and somatosensory systems were perturbed simultaneously. Importantly, the degree of freedom in both males and females in the present study could be used as a fundamental reference for identifying the progress in motor leaning (Guimarães et al., 2020) in pathological groups, such as patients with vestibular disorders or in astronauts in the future.

4.3 The interaction between the sex effect and VS effect

As far as we are aware, this was the first study to investigate the interaction between the sex effect and the VS effect on balance control regardless of whether the participants were standing in SOT1 or SOT5. It is interesting to note that females increased PR of CoG in the ML direction regardless of whether unilateral or bilateral VS was applied. In contrast, males increased PR of CoG in the ML direction only when unilateral VS was applied. Furthermore, only unilateral VS increased the SampEn of CoG in the ML direction in females whereas none of the VS affected the SampEn of CoG in males. Three observations need to be addressed with regard to these findings: 1) why did VS only affect balance control in the ML direction, but not in the AP direction, 2) why did VS have a greater effect on balance control in females than in males, 3) why did unilateral VS appear to affect SampEn of CoG more than bilateral VS in females than in males? Baudy and Kuo (2000) explain the first observation by the fact that balance control was more difficult in the ML direction than in the AP direction. It was possible that the second observation can be substantiated by the fact that females were more sensitive to vestibular signals than males (Sung et al., 2011; Battersby, 2019; Schubert et al., 2022). Third, despite standing normally with visual support, unilateral VS, but not bilateral VS, significantly increased the SampEn of CoG in the ML direction in older adults. In Lin et al., 2022 explanation, the deterioration of the vestibular system by aging caused older healthy adults to compensate for the disruption in the unilateral vestibular system by increasing their degree of freedom in the ML direction. As shown in the present study, it is not necessary to explain the phenomenon by a deterioration of vestibular function, rather, the higher sensitivity of vestibular system in females than in males was more likely to be the cause. These results confirmed the feasibility to use the VS to identify the differences in balance control between males and females, which has been used to identify the differences in balance control by aging (Lin et al., 2022). Therefore, it might be possible to apply this VS technology to identify the vestibular-related

balance control in patients with various types of vestibular disorders and astronauts.

4.4 The interaction among SOT condition effect, sex effect and VS effect

When it comes to discussing the interaction between SOT condition effect, sex effect and VS effect, it has been found that PR of CoG in the ML and total CoG traveling distance in the AP direction were significantly different between males and females when standing in the most challenging condition (SOT5) with bilateral VS. Specifically, males demonstrated a greater total CoG traveling distance in the AP direction than females; however, females showed a greater PR of CoG in the ML direction than males in such a challenging condition. It is important to note that the total CoG traveling distance and the PR of CoG have been interpreted differently. The total CoG traveling distance represented the total amount distance the CoG travels; however, the PR of CoG indicated the sum of amplitude of instantaneous CoG travelled compared to the maximum amplitude of CoG travelled. On one hand, the greater body mass and height of males, according to Greve et al.'s (2012) study, explain greater total body travel distance than that of females while standing in such a challenging condition. On the other hand, it must be taken into consideration that the greater amplitude of the instantaneous CoG traveled in a vestibular-disturbed and vestibular-demanding environment might increase the potential risks of falls for females.

4.5 Conclusion

The sex effect on vestibular function in astronauts generally has been ignored because most astronauts are males. As NASA intends to send a female to the Moon in 2024, it is essential to clarify how women differ from men when it comes to balance control while standing in a vestibular-demanding and unpredictable environment. As a result of the present study, it can be concluded that in the future, when performing space missions or evaluating vestibular function pre- and post-spaceflight, the sex effect must be taken into consideration. In addition, one strength of this study was the use of the VS as an unpredictable vestibular disruption in order to assess the sex differences in standing on an environment that is vestibular-demanding. It was also a strength of this study that multiple practical approaches were employed in order to quantify balance control in sensory-conflicted conditions. These results could serve as fundamental references for future comparisons of balance control between pathological groups and astronauts.

4.6 Limitations

There were a couple of limitations in the present study and need to be performed in the future:

- The purpose of the present study was to examine the sex differences in vestibular-related balance control while standing, rather than when walking, where frequent falls

are more likely to occur. It is necessary to conduct further studies to examine the sex effect on vestibular-related balance control when walking in vestibular-demanding and vestibular-disrupted environments.

- Considering that no sensorimotor training was conducted in the present study, it is unknown whether training in such vestibular-demanding and vestibular-disrupted conditions would enhance the ability to maintain balance control in unpredictable environments. This question needs to be addressed in future studies.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary Material](#), further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by the University of Nebraska Medical Center (IRB Protocol # 379-17-EP). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

LZ: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Writing—original draft, Writing—review and editing. CQ: Supervision, Validation, Writing—review and editing. JC: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Visualization, Writing—original draft, Writing—review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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Challenges and support needs in psychological and physical health among pilots: a qualitative study

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Introduction: Physical and mental health problems among pilots affect their working state and impact flight safety. Although pilots' physical and mental health problems have become increasingly prominent, their health has not been taken seriously. This study aimed to clarify challenges and support needs related to psychological and physical health among pilots to inform development of a more scientific and comprehensive physical and mental health system for civil aviation pilots.

Methods: This qualitative study recruited pilots from nine civil aviation companies. Focus group interviews via an online conference platform were conducted in August 2022. Colaizzi analysis was used to derive themes from the data and explore pilots' experiences, challenges, and support needs.

Results: The main sub-themes capturing pilots' psychological and physical health challenges were: (1) imbalance between family life and work; (2) pressure from assessment and physical examination eligibility requirements; (3) pressure from worries about being infected with COVID-19; (4) nutrition deficiency during working hours; (5) changes in eating habits because of the COVID-19 pandemic; (6) sleep deprivation; (7) occupational diseases; (8) lack of support from the company in coping with stress; (9) pilots' yearly examination standards; (10) support with sports equipment; (11) respecting planned rest time; and (12) isolation periods.

Discussion: The interviewed pilots experienced major psychological pressure from various sources, and their physical health condition was concerning. We offer several suggestions that could be addressed to improve pilots' physical and mental health. However, more research is needed to compare standard health measures for pilots around the world in order to improve their physical and mental health and contribute to overall aviation safety.

KEYWORDS

occupational health, mental health, physical health, qualitative study, pilots and cabin crew, COVID-19

1 Introduction

It is known that pilots' health affects their working state. However, the serious risks posed by pilots' working conditions, including enclosed cabins that are exposed to ultraviolet radiation at high altitudes for long periods (1) and isolation rooms during the COVID-19 pandemic, mean that pilots' physical and mental health problems have become increasingly prominent; these health problems may impact flight safety (1–4). Previous studies have reported that compared with well-rested people, pilots who felt tired from lack of sleep thought and reacted more slowly, had more memory problems, and were more likely to make mistakes (5–7). The [PlaneCrashInfo.com](https://www.plane-crash-info.com) database shows that approximately 50% of flight accidents are related to pilots' working state; this proportion has not changed significantly over time. These data confirm that pilots' physical and mental health impact flight safety by affecting their working state. Therefore, improving pilots' physical and mental health is necessary to improve aviation safety (7).

Previous studies have shown that common health problems among pilots include abdominal distension, headache, fatigue, and depression, attributable to factors such as smoking, drinking, and irregular diet and sleep (6, 8–10). Increased use of caffeine, alcohol, and drugs cannot prevent deterioration of physical and mental conditions but increases the risk for insomnia and sleepiness, whereas exercise can effectively improve pilots' physical and mental health (6, 11). Most previous studies on this topic were conducted using questionnaires, which could not accurately capture pilots' subjective feelings (1–6). Qualitative research in this area is relatively scarce, meaning personalized information about pilots' feelings remains largely unknown. In addition, most previous studies have focused on physical or psychological evaluations. However, both physical and mental health are important components of overall health, and can influence each other; therefore, a discussion combining physical and mental health may provide a more comprehensive perspective on pilots' health issues. Unfortunately, many unilateral studies could not effectively link these two aspects to draw comprehensive conclusions. In contrast, this study used a comprehensive qualitative approach with data collected in interviews. This allowed us to pay attention to pilots' real experiences, rather than constraining these experiences using set response options. Additionally, using focus group interviews meant that we could analyze pilots' perspectives of challenges and support needs in relation to both physical and mental health aspects, which allowed a comprehensive analysis.

In this qualitative study, we hoped to offer preliminary mind mapping of pilots' basic working conditions based on pilots' experiences of their psychological and physical health through interviews. We aimed to analyze the experiences expressed by pilots in relation to various factors, such as energy and time distribution between work and life, exercise habits, diet and sleep regularity, pressure conditions, and the impact of the pandemic on work content and income. This allowed us to summarize pilots' experiences of their profession, examine their perspectives of their own health, and explore their real support needs. The purpose of this series of qualitative focus group interviews was to clarify the challenges faced by pilots relating to both physical and mental health, and determine pilots' needs and suggestions from the perspective of balancing physical and mental

health. Ultimately, this study may provide guidance for follow-up intervention research to improve the relevance and effectiveness of strategies to improve pilots' mental and physical health. Our overarching purpose was to provide pilots with more appropriate psychological and physical health support.

2 Materials and methods

Focus group interviews were carried out via the Tencent conference platform. Interviewed participants' statements about their experiences on career-related topics were used as the data for analysis. COREQ guidelines were used to guide this study (12).

2.1 Study sample

A purposive sampling method was used to select pilots from nine civil aviation companies: two large, three medium-sized, and three small civil aviation companies and one cargo airline (which is a special type of civil aviation company). We randomly selected three or six pilots from each airline and conducted interviews in batches of three participants. The reason for selecting three participants for each focus group interview was that the privacy and duration of the interviews would have been difficult to control with more participants, and the information collected might have been incomplete with fewer participants. Participant selection was stratified by age and position (copilots: including pilot cadet and second copilot, and captains or squadron leaders) to cover all sub-groups of pilots. The inclusion criteria for this study were that participants must be actively employed as pilots and reside in East China. Any pilot that withdrew during the interview process was excluded from the valid sample. We considered the problem of information saturation, and the sample size and interview content were determined based on this principle. In total, we interviewed 42 pilots (Table 1). All participants provided informed consent before their interviews.

Participants belonging to the same company were allocated to the same interview group, with each group comprising three participants. Overall, 14 groups were formed and interviewed successively.

2.2 Ethical considerations

This study was approved by the Ethics Committee of Civil Aviation Shanghai Hospital (no. 2021-7). All ethics procedures and governance requirements were adhered to for each interviewed participant. All participants were advised that participation was voluntary, they had the option to withdraw from the study, and the interview session could end at any time they requested without any repercussions.

2.3 Data collection

The interview outline was developed by the research team after reviewing relevant literature (13, 14), and reflected our purpose of improving pilots' physical and mental health. The outline focused on

TABLE 1 Participants' general information.

Serial number	Gender	age	Date of interview	Position	Serial number of company	Marital status	Record of formal schooling	Years of flight
1	Male	35	2022.8.8	Squadron leader	1	Married	Undergraduate course	13
2	Male	34	2022.8.8	Squadron leader	1	Married	Undergraduate course	11
3	Male	37	2022.8.8	Squadron leader	1	Married	Undergraduate course	15
4	Male	36	2022.8.9	Squadron leader	2	Married	Undergraduate course	14
5	Male	55	2022.8.9	Squadron leader	2	Married	Undergraduate course	18
6	Male	48	2022.8.9	Squadron leader	2	Married	Undergraduate course	22
7	Male	34	2022.8.9	Squadron leader	3	Married	Undergraduate course	6
8	Male	36	2022.8.9	Squadron leader	3	Married	Undergraduate course	8
9	Male	42	2022.8.9	Squadron leader	3	Married	Undergraduate course	14
10	Male	40	2022.8.10	Squadron leader	4	Married	Undergraduate course	14
11	Male	38	2022.8.10	Squadron leader	4	Married	Undergraduate course	13
12	Male	39	2022.8.10	Squadron leader	4	Married	Undergraduate course	13
13	Male	52	2022.8.10	Squadron leader	5	Married	Undergraduate course	18
14	Male	40	2022.8.10	Squadron leader	5	Married	Undergraduate course	18
15	Male	42	2022.8.10	Squadron leader	5	Married	Undergraduate course	17
16	Male	30	2022.8.10	Copilot	6	Married	Undergraduate course	3
17	Male	27	2022.8.10	Copilot	6	Unmarried	Undergraduate course	0.5
18	Male	30	2022.8.10	Copilot	6	Unmarried	Undergraduate course	3
19	Male	30	2022.8.11	Copilot	4	Unmarried	Undergraduate course	3
20	Female	29	2022.8.11	Copilot	4	Unmarried	Undergraduate course	3
21	Male	26	2022.8.11	Copilot	4	Unmarried	Undergraduate course	1
22	Male	43	2022.8.11	Squadron leader	7	Married	Undergraduate course	22
23	Male	45	2022.8.11	Squadron leader	7	Married	Undergraduate course	22
24	Male	43	2022.8.11	Squadron leader	7	Married	Undergraduate course	22
25	Male	32	2022.8.11	Copilot	8	Married	Undergraduate course	6
26	Male	31	2022.8.11	Copilot	8	Married	Undergraduate course	3
27	Male	27	2022.8.11	Copilot	8	Unmarried	Undergraduate course	3
28	Male	47	2022.8.15	Squadron leader	9	Married	Undergraduate course	23
29	Male	42	2022.8.15	Squadron leader	9	Married	Undergraduate course	20
30	Male	46	2022.8.15	Squadron leader	9	Married	Undergraduate course	21
31	Male	40	2022.8.16	Squadron leader	7	Married	Undergraduate course	19
32	Male	39	2022.8.16	Squadron leader	7	Married	Undergraduate course	15
33	Male	40	2022.8.16	Squadron leader	7	Married	Undergraduate course	19
34	Male	28	2022.8.16	Copilot	9	Unmarried	Undergraduate course	5
35	Male	25	2022.8.16	Copilot	9	Unmarried	Undergraduate course	5
36	Male	24	2022.8.16	Copilot	9	Unmarried	Undergraduate course	3
37	Male	49	2022.8.17	Squadron leader	8	Unmarried	Undergraduate course	23
38	Male	42	2022.8.17	Squadron leader	8	Unmarried	Undergraduate course	17
39	Male	43	2022.8.17	Squadron leader	8	Unmarried	Undergraduate course	20
40	Male	39	2022.8.17	Squadron leader	6	Married	Undergraduate course	15
41	Male	42	2022.8.17	Squadron leader	6	Married	Undergraduate course	17
42	Male	38	2022.8.17	Squadron leader	6	Married	Undergraduate course	18

participants' working experience, living habits, and challenges in work and life. To optimize timely data collection, the research team conducted simulated interviews with two non-aviation practitioners

and then modified the interview outline as necessary to avoid questions perceived as intruding on participants' privacy or that had unclear meanings.

2.3.1 Final interview outline

Q: You mostly work in the cabin of an airplane. Do you feel that it interferes with your leisure and family life? Are there fewer opportunities to exercise?

Q: In terms of diet, are your main meals served by the crew? Do you get bored and want something else for a change?

Q: It appears that your working hours are largely limited by the flight schedule. Is this a stressful working mode? What is your schedule like? How do you feel about your sleep? Have you experienced a sleep disorder (e.g., difficulty falling asleep, waking up at night, waking up early in the morning)?

Q: Does the stress from work interfere with your daily life?

Q: In the past 2 years, the airline industry was greatly affected by COVID-19. What were the differences between your working pattern during that period and non-COVID-19 times? Has the pandemic affected your income? Do you feel more stressed and anxious?

Q: In such a unique period, did you have a different view of work than before? Could you share your opinion on the measures taken by your country or your company for COVID-19 prevention, protection, and quarantine management? Does the company provide psychological counseling and other interventions? How does it work?

2.3.2 Research protocol

Before the interviews, one researcher (M.X.) had preliminary contact with participants through WeChat and invited them to participate in the online focus group interviews via the Tencent conference platform. Only the research team members and participants attended the group interviews. Before each interview started, the interviewers introduced the research team members (including the name, identity, and responsibilities of each member) and the purpose of this qualitative research. The research team's commitment to confidentiality of the interview data was also clearly stated. Consent was then obtained from all participants. All interviews were conducted in Chinese and then translated and reviewed by W.X. and Y.B. for inclusion in this manuscript.

2.3.3 Interview process and reflection

As most participants were male, the interviews were mainly conducted by two male interviewers (Y.B. and H.H.), supplemented by questions from the supervising researcher. During interviews, the interviewers and participants turned on their cameras and enabled voice communication. The interviews were recorded to facilitate the subsequent arrangement of the interview results. Each interview lasted 45–90 min.

To improve the interview quality and ensure information saturation, members of the interview team analyzed and reflected on the problems encountered in the interview process and put forward practical suggestions after each interview.

2.4 Data analysis

Step 1: after the interviews, the researchers immediately transcribed the recordings. Colaizzi's 7-step method was used for data analysis (15). We repeatedly read the interview materials to understand the general meaning.

Step 2: we extracted statements of significance and then coded recurring, meaningful ideas.

Step 3: we summarized the encoded ideas, which was followed by writing a detailed description without omissions.

Step 4: we then refined similar views and developed the theme concept.

Step 5: the analysis results were returned to participants for validation. In cases of disagreement, the research team resolved problems through discussion to ensure the accuracy of the results.

3 Results

Forty-two pilots from nine civil aviation companies (two large civil aviation companies, three medium-sized civil aviation companies, three small civil aviation companies, and one cargo airline) participated in the interviews. Most participants were captains (71%), and the remainder were copilots or flying cadets (29%). The majority of participants were aged over 35 years (64%), male (98%), married (71%), and had over 10 years of flying experience (67%). All participants had completed their undergraduate education (Table 2).

We identified three major themes from the interview data that covered the main types of issues reflected in participants' narratives and the magnitude of their impact: (1) psychological stress; (2) physical health; and (3) pilots' needs and suggestions.

3.1 Psychological stress

3.1.1 Imbalance between family life and work

Some participants expressed that their stress originated from the lack of work-family balance. Pilots faced long-term absences from their families because one cycle of their flying assignments usually took several days (or more), and each interval between flying tasks was relatively short.

"Even after returning home, I may have to start a new round after several days, and the number of days I can return home might be only dozens of days in a year. In these days, there must be a lot of things to deal with. For people around our age, the biggest worry is the health of the older adults and children. Once they get sick, you can only rely on your spouse to take care of the four older adults and one child; even some second-child families will have two children, which is a greater pressure for the spouse. Some of our colleagues' spouses will quit their jobs to be stay-at-home mothers for the sake of their families, which is also unfair to their spouses. They give up their careers for the sake of their families." (male, 36 years, captain)

3.1.2 Pressure from assessment and physical examination eligibility requirements

Some participants who were flying cadets found it difficult to complete their assessment to a high standard. The fear of making mistakes created major pressure, which resulted in serious psychological stress in the long term.

“When you’re in the cadet stage, the standard might be asking you to finish 40% of the job correctly, but the faculty is asking you to finish 60% of it correctly. They themselves might be able to do 90%, or even 100% of the job, without any mistakes. However, this is actually very difficult for us. Suppose you want to do 100 things, to make 10 to 20 mistakes is very easy, but if you allow yourself to make only one mistake, or not make any mistakes, it ends up being very difficult.” (male, 26 years, copilot)

Some participants emphasized that the physical examination, which was an essential part of their yearly assessment, also caused psychological stress. This was because failure to meet the physical examination standards implied a potential significant safety risk, which would directly result in suspension of that pilot’s medical certificate.

“We have a hard target to meet in our physical examination every year. If we fail to meet the target, our work arrangement will be affected.” (male, 30 years, copilot)

Given the stress caused by the various assessments, pilots reported experiencing a heavy psychological burden, especially older pilots. With all these stress from the various assessments, pilots reported heavy psychological burden, especially in older pilots. This finding provides a theoretical basis for the development of intervention to improve the mental health of pilots.

3.1.3 Pressure caused by worries about being infected with COVID-19

Most participants reported that the COVID-19 pandemic had a huge influence on the civil aviation industry and on pilots themselves. They noted that the pressure experienced during the COVID-19 pandemic originated from the economic pressure caused by the decreased flying time, continuous isolation, and fear of contracting the virus.

“Meanwhile, the flights have reduced a lot since the COVID-19 pandemic, and now about half of them are cancelled. Many captains have a lot of pressure regarding mortgage payments especially during the lockdown period. Now, to most of the young people, even the captain, especially those whose home is not here in Shanghai, the pressure is rather big. There are so many family members that they need to take care of, parents, children, and so on. They could probably handle it before the pandemic, but now they lack confidence.” (male, 48 years, captain)

“Another point causing anxiety for our pilots is COVID-19 because we have to stop flying immediately when we are found to be infected in the physical examination. We have to wait until the nucleic acid test is negative, then be observed on the ground for 2 or 3 months and wait for the Civil Aviation Administration of

China (CAAC) to make a decision. The whole process may last for 6 months. (...) Though we’re all under close management, and we’ve all taken precautions, Omicron is highly contagious with many variants, so there’s still a lot of risk. And if we get infected, we stop flying, which makes us very anxious.” (male, 36 years, captain)

3.2 Physical health

3.2.1 Nutrition deficiency during working hours

Most participants shared that prepared airline meals during flight tasks created a serious problem regarding nutrition deficiency. They noted that this problem originated from three phenomena: irregular meal timings, imbalanced nutrition structure of prepared airline meals, and limited choice.

Many participants reported they had an irregular diet during flight tasks, which was closely related to the flight and landing times. This made it difficult for pilots to get sufficient nutrition when needed, which may harm their health.

“The total life schedule of our occupation is irregular because it is based on the time of the flight. For example, there are early or late flights sometimes. Under such circumstances, maybe some of the pilots do not follow the schedule in terms of diet. (...) For us, especially when the flight time is right around lunch time or dinner time, what we can do is simply postpone the time to eat or finish having meals in an extremely short time.” (male, 36 years, captain)

Most participants claimed that the nutritional structure of the airline meals could not be guaranteed. Although basic nutritional factors (e.g., the amount of energy, vitamins) were considered carefully

TABLE 2 Participants’ demographic characteristics.

Characteristics	Numbers	Percentage
Sex		
Women	1	2%
Men	41	98%
Age, years		
<35	27	64%
≥35	15	36%
Marital status		
Married	30	71%
Unmarried	12	29%
Record of formal schooling		
Undergraduate course	42	100%
Position		
Captain	30	71%
Copilot	12	29%
Years of flight, years		
<10	14	33%
≥10	28	67%

when the meals were prepared to ensure that the pilots were well-conditioned and make the flight safe, the quality of the meals varied from company to company. Some participants reported high levels of salt and oil in their airline meals.

Many participants reported a tendency to overeat when finishing a flying task. Participants' narratives emphasized that they tended to choose unhealthy foods as a kind of "compensation" for the prolonged intake of bland foods during flying tasks.

"After landing, most people really will go and overeat, and will be more likely to eat some food with strong flavor, such as spicy hot pot. Most of us know very well that this food is not healthy, but we really want to eat it." (male, 27 years, copilot)

Some participants added that the limited choice of airline meals was a major problem for many pilots with allergies. For example, if airline meals happened to include allergens, most pilots had no choice but to skip the meal, which resulted in inadequate energy and nutrition intake, which could potentially damage the digestive system in the long term (16).

"There are a lot of people who are lactose intolerant, or allergic to legumes or other foods, so for those people there is little choice." (male, 28 years, copilot)

Some participants expressed that it would benefit their physical and psychological health if the airline meals were more balanced in terms of nutrition. A similar request was also made in relation to meals provided during isolation periods because of the COVID-19 pandemic, as meals during quarantine were often provided by the airline for safety reasons. Moreover, some participants noted that more personalized meals or more choices in the daily meals may increase their desire to eat airline meals, which would prevent the lack of nutrition resulting from reluctance to eat airline meals. Several participants advised that the taste of the airline meals could also be improved to make pilots more willing to eat these meals to guarantee sufficient nutrition intake.

"All the quarantine hotels are short of vegetables. Because of the epidemic, we cannot buy materials from the outside, so we hope the company can intervene to provide us with some vegetables. Now there is an imbalance between meat and vegetables, and there is not much choice." (male, 28 years, copilot)

3.2.2 Changes in eating habits because of the COVID-19 pandemic

Some participants emphasized that their diet during the COVID-19 pandemic differed from that before the pandemic. On the one hand, the decreased flying time meant that pilots had more time to spend at home, which resulted in the normalization of daily diets. On the other hand, there were periods of isolation after finishing flights. The meals during this period were supplied by the company and were the same as the prepared airline meals, so there were still problems such as nutrition imbalance and limited choice.

"During the period of isolation, we mainly ate boxed lunches from the hotel, which was also arranged by the company. Some of them were greasy and not that healthy." (male, 48 years, captain)

3.2.3 Sleep deprivation

Although some participants said that sleep problems were within their range of self-regulation, about a half of the participants acknowledged that sleep deprivation often occurred, especially on morning and evening flights.

"There will be some cases of insomnia more or less. (...) They may sleep at home during the day before the flight so that they have more energy at night, but later they find that it is not appropriate as they can't sleep in the morning after the night flight. Then some people will stay up in the morning, so that they can sleep better at night, but they still can't make up for the lost sleep." (male, 42 years, captain)

Some participants from large civil aviation companies with international airlines also reported that jet lag was a major problem which affected the quality of their sleep (17).

"The body is used to it. It can't sleep when it's time to sleep. It can't rest when it's time to rest." (male, 52 years, captain)

3.2.4 Occupational diseases

Participants expressed that the damage to their physical health originated from multiple occupational diseases. Most interviewed pilots had lumbar spondylosis and cervical spondylosis, which they attributed to sitting for too long and the discomfort of the cockpit seat. Several participants believed that working at high altitude for long periods of time could lead to various diseases such as heart disease, attributed to changes in radiation and air pressure at high altitude. A minority of participants reported they suffered from conditions such as hair loss, lithiasis, and high blood pressure, which may be closely related to dietary limitations during flight assignments. Two pilots reported that they suffered from shoulder arthritis, migraines, bloating, and debilitating mental problems. A female pilot also reported delayed menstruation.

"It's not just sitting, it's related extension issues, like cervical spondylosis, noise, that actually have a physiological impact all the time." (male, 42 years, captain)

"The relative low pressure of the upper air and internal and external pressure difference may affect viscera organs and ear pressure." (male, 46 years, captain)

"High blood pressure, lithiasis and so on may have something to do with flying, because for a long time on the plane we just sit there, rarely get up and do some activities, which may be some objective factors. It is hard to say is directly caused, but also have to say that this will bring about physical symptoms." (male, 55 years, captain)

"After working for a certain time, sometimes you will find that menstruation becomes delayed or irregular." (female, 29 years, copilot)

3.3 Pilots' needs and suggestions

3.3.1 Lack of support from the company in coping with stress

Most participants claimed that they experienced difficulty in releasing their psychological stress and required a workable approach to handle this stress. Participants mentioned that they worried about the impact on their career if they used psychological support provided by the company, which reduced the effectiveness of that support. That is, pilots wanted support options that did not involve the company. Participants noted that pilots tended to have a relatively small circle of friends, mainly limited to family and colleagues, so it was hard for them to find someone to talk to when dealing with psychological stress. In short, most participants expressed a desire for more chances to communicate and release their pressure without worrying that their complaint would become known to the company and therefore influence their career. This support was expected to be provided by a third party in the context of wider society.

"Many people may only be able to relieve stress through self-adjustment or through some communication with their regular colleagues. (...) Human beings are social animals. I think if we can have more opportunities to communicate and express our pressure, the effect may be better." (male, 45 years, captain)

3.3.2 Pilots' yearly examination standards

One participant noted that the standards for physical examination were still the same as they were decades ago, which did not reflect the changes in public health. Therefore, he suggested updating the physical examination standards based on pilots' current general health condition.

"The physical examination standards for pilots are still the same as they were 30 or 40 years ago. Considering the human health index has changed generally now, the standards should be adjusted appropriately as well." (male, 47 years, captain)

3.3.3 Support with sports equipment

Some participants reported a need for financial support to buy sports equipment, as the sports/activity facilities supported by the company often took too much time to access. Some participants advised that the company could try different methods such as providing gym cards or sports equipment vouchers.

"The company has some measures anyway. There are gyms, physical therapy rooms, and so on but you have to use your commute time to get there from home." (male, 34 years, captain)

"I hope the company can reimburse a little sports equipment every year, such as for basketball, volleyball, and so on." (male, 34 years, captain)

3.3.4 Respect planned rest time

Participants noted the need for more rest time. Most companies had adopted the "2-day rest after 3-day flight" pattern, but participants explained that during the "2-day rest" period, they were required to handle extra work such as flight preparation and some administrative

work. They expressed that the company required them to fly as often as possible to earn more benefits to the company, which resulted in high fatigue conditions. Vacations rostered by the company were usually inadequate for them to recover. However, because of their income, they did not want to take extra leave to get a thorough rest. Therefore, they hoped that they could have more paid vacation time that could give them the chance to relax completely.

"We usually fly for 3 days and then have a rest for 2 days, but we still have to go to work at the company during these two days, because we still have a lot of groundwork and administrative work to do, so it is still a busy situation. Sometimes I feel tired, but I still have to fly for 3 days. After all, I don't get paid if I don't fly." (male, 47 years, captain)

"We hope that we can learn something from Western management. Western countries have a system of paid vacation. It seems very insignificant, but people can be completely relaxed in this situation." (male, 40 years, captain)

3.3.5 Isolation periods

Moreover, as our interviews were conducted during the COVID-19 pandemic period under a strict isolation policy, most participants reported long isolation periods after each flight, which often lasted for 2 weeks to several months. These periods of isolation during the COVID-19 pandemic were considered too long. Many participants stated that the isolation could be shortened as the long-term isolation directly led to their anxiety.

"I suggest that the isolation period be reduced appropriately and the 4+3 mode (i.e., 4 days of centralized isolation and 3 days of home isolation) be adopted." (male, 48 years, captain)

4 Discussion

In this qualitative study, participating pilots described various psychological and physical health challenges. These challenges had implications for pilots' well-being and at last flight safety.

4.1 Psychological health

In our study, participants reported multifactorial stressors related to the absence from their family, assessments, and the COVID-19 pandemic. The main stressors among pilots varied across different age groups. Stress among younger pilots mainly originated from their financial situation, promotion opportunities, and social interactions, whereas that among older pilots mainly arose from concerns about their health and being absent from their families. The differences in stressors between older and younger pilots may be because an individual's self-perception of aging and their physical condition becomes worse with age, which in turn leads to deterioration of health (18). In addition, older pilots tended to attach more importance to family, meaning that their absence from family life became a significant source of stress. Our results were consistent with some previous studies that also emphasized that stress among younger pilots mainly resulted from

worries about income and promotion and led to mental health issues (19, 20). Conversely, mental health issues among older pilots tended to originate from being absent from their families. A previous study highlighted the importance of being accompanied by family members to improve mental health (21). In addition, a study focused on stressors experienced by Chinese pilots highlighted that the risk of income reduction, contracting COVID-19, stress at work, and the risk for a delayed upgrade schedule were major mental health stressors during the COVID-19 pandemic (20).

Various promising methods could be considered by civil aviation companies to improve pilots' mental health. For example, given the financial pressure pilots faced during the COVID-19 pandemic because of reduced flights, airlines could provide pilots with more care focused on daily life (20, 22). In addition, measures to guarantee pilots' family security may offer a promising solution to relieve mental health pressures caused by long periods of absence from their families during the COVID-19 pandemic, such as providing subsidies to families for daily necessities during pilots' isolation periods. Participating pilots mentioned that various limitations still existed despite civil aviation companies attempting to improve staff mental health, such as by establishing psychological counseling rooms. Although most companies had a counseling room, most pilots preferred not to use these services because they feared doing so would negatively affect their future careers. Instead of psychological support directly provided by the companies, social support may provide an effective solution to improve pilots' psychological health, which was demonstrated in a previous study (23). Economic support for pilots' careers and families and some appropriate social support may also help to relieve their stress, thereby improving pilots' mental health, especially during the COVID-19 pandemic.

4.2 Physical health

Our findings highlighted that a poor diet, poor sleep quality, and occupational diseases were the main factors affecting pilots' physical health based on their self-report. Participants commented on the irregular and high-salt diet when completing flight tasks or isolation periods, which they believed was harmful to their physical health. Research shows that irregular diets can increase the risk for esophageal and stomach cancer (22). The high-salt diet reported by some participants increased the possibility of high blood pressure, cardiovascular disease, and stroke (24). Sleep problems are common among pilots; for example, a previous survey found 24.6% of short-haul and 23.5% of long-haul pilots reported major sleep problems 8 nights a month (3). Furthermore, previous studies found that pilots' health problems were mainly in the cervical, shoulder, and lumbar spine, such as cervical spondylosis, periartthritis of the shoulder, reflex shoulder, arm and hand pain, swelling and numbness, back and leg pain, lumbar disc herniation, and lumbar muscle strain (10, 25–28). These factors were also reported in our interviews. In addition to those diseases, our participants reported problems such as hyperlipidemia, hypertension, dyspepsia, lithiasis, endocrine dysfunction, and neurasthenia.

The emphasis on physical health problems reported by different age groups also differed. Generally, younger pilots reported more cases

of diet problems, whereas older pilots reported more sleep problems. Occupational diseases were common among pilots but more pronounced among older pilots, which was consistent with the results of a previous study (19). This may be because most occupational diseases that pilots are prone to are chronic (29). For example, a study on lipid status among pilots found that high triglycerides and total cholesterol levels among pilots were related to older age and longer flight time (30).

From a physical health perspective, most participants expressed an urgent need for more choice of meals and more rest time. It is worth noting that companies should place more consideration on the cost of welfare measures (e.g., time and convenience), which may influence whether pilots are willing to use these measures. For example, the company could organize regular physical examinations for cardiovascular problems, which are common among pilots, and offer medical care or convalescent leave to pilots with poor results. Moreover, airlines could design reasonable and scientific flight schedules to guarantee sufficient sleeping time. More attention should also be paid to nutritional composition when preparing airline meals.

4.3 Implications

Our results have some practical implications that may help civil aviation companies and air transport management departments to improve pilots' physical and psychological health. Currently, the aviation medical field lacks a scientific and comprehensive assessment method for civil aviation pilots (31–33), including factors such as physical health, mental health, and healthy behaviors, as well as a dynamic monitoring platform and health management system for health data in this field. Many physical or psychological assessment methods conducted for individuals or other occupational groups are not suitable for pilots because pilots receive special learning and training, and their working conditions differ from those to which others may be exposed (31, 32). Furthermore, relatively little research has been conducted on civil aviation pilots' physical and mental health, with a notable lack of high-quality research (20, 34, 35). Most available studies were based on scales, questionnaires, or standardized questions (1–6). Therefore, we attempted to capture pilots' perspectives of their physical and mental health-related challenges and needs through face-to-face conversations via qualitative interviews. This allowed us to confirm information or seek clarity during the interviews to ensure accuracy. We comprehensively collected the information provided by participants during the interviews and paid equal attention to each participants' personalization, meaning our results are rich and specific. Our study will provide evidence to inform the development of a more scientific and comprehensive physical and mental health evaluation system for civil aviation pilots. This will help to achieve "early detection, early prevention, early intervention, and early treatment." Through the development of all-round, multi-dimensional, and different life cycle stages of "health portraits," it is possible to promote safer management of civil aviation pilots' physical and mental health and reduce the occurrence of physical and mental health damage.

4.4 Limitations

There were some limitations in this study. First, because of the serious imbalance in the male to female ratio in the occupational group of pilots, only one female participant was interviewed; therefore, our study might not be representative of the experience of female pilots. However, only 0.44% of airplane pilots in China are women, as reported in the Annual Report of Chinese Civil Aviation Pilot Development (36); therefore, our study provided relatively robust evidence regarding the challenges of pilots' psychological and physical health. Second, because the interviews were mainly conducted in groups, some questions, especially those that touched on participants' privacy, could not be explored in-depth. A further study using individual interviews is needed to resolve this issue. Third, the purpose of our study was to investigate pilots' health conditions; therefore, comparisons among companies were relatively weak and more evidence is needed. For example, we did not explore the differences in welfare benefits between companies, so we could not determine the relationship between differences in these benefits and pilots' various needs. We intend to conduct further research in this area. Finally, our study investigated pilots' health challenges and needs through focus group interviews. Although this method meant that personalization was emphasized compared with questionnaire surveys, the results could not be quantified, and it was not possible to analyze the correlations between various factors and the results or the correlations between various factors. In addition, this study was based on self-reported information, and the results obtained may be biased because of individual differences in expression. Obtaining accurate data (e.g., physical examination results) was also difficult. Therefore, we need to combine other research methods in a further study to improve the accuracy of the results.

5 Conclusion

In this study, we interviewed 42 pilots and found that they experienced a large amount of psychological pressure from various factors. Their physical health condition was also worrying, and pilots had several suggestions in relation to improving their physical and mental health. Although pilots are generally satisfied with the working environment, they are aware that the schedule and content of their work can have a negative impact on their physical and mental health. In addition, the COVID-19 pandemic situation and the lack of suitable professional assessment are also health-related problems that remain to be resolved. Civil aviation companies, air transport management departments, and aviation hospitals pay insufficient attention to pilots' physical and mental health. Therefore, it is necessary to establish a systematic, scientific, and personalized medical intervention system for pilots going forward. Through this qualitative study, we identified pilots' perspectives of challenges and support needs in relation to psychological and physical health, and also laid a foundation for subsequent research. We hope to attract more researchers to conduct comparative studies of standard health measures for pilots in different parts of the world. This will provide a reference for civil aviation companies and governments worldwide to support improvement of pilots' working conditions, which will ultimately improve pilots' physical and mental health and contribute to overall aviation safety.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Ethics Committee of Civil Aviation Shanghai Hospital (no. 2021-7). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

WX: Data curation, Writing – review & editing, Writing – original draft. YB: Data curation, Writing – review & editing, Writing – original draft. LZ: Data curation, Writing – review & editing. YL: Data curation, Writing – review & editing. EZ: Data curation, Writing – review & editing. HL: Data curation, Writing – review & editing. QJ: Data curation, Writing – review & editing. YC: Data curation, Writing – review & editing. QD: Data curation, Writing – review & editing. FS: Data curation, Writing – review & editing. LW: Data curation, Writing – review & editing. ZL: Data curation, Writing – review & editing. XC: Data curation, Writing – review & editing. QG: Data curation, Writing – review & editing. HH: Data curation, Writing – review & editing. BR: Data curation, Writing – review & editing. YS: Data curation, Writing – review & editing. MX: Data curation, Supervision, Writing – review & editing, Investigation, Project administration.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The effect of Ashtanga-Vinyasa Yoga method on air force pilots' operational performance

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Introduction: In today's military landscape, optimizing performance and bolstering physical health and mental resilience are critical objectives. Introducing a 12-week Ashtanga Vinyasa Yoga Supta Method (AVYSM) to the training protocol of military trained Airforce pilots, we aim to assesses the feasibility and impact of the method.

Materials and equipment: Borg Scale assesses the intensity level of physical activity during the intervention. Flight simulator data gauges operational performance responses. Postural control responses are measured using a force platform, stress responses are monitored via heart monitor, and handgrip dynamometry will measure strength. Respiratory capacity is assessed using a spirometer, body composition is evaluated using impedance balance, and aviation-related questionnaires are administered before and after the intervention period.

Methods: In a randomized controlled trial, the totality of pilots from the "Masters in Military Aeronautics: aviator pilot specialist" course at the Portuguese Air Force Academy (PAA) were randomly assigned to the yoga intervention or the waiting list control groups, with participants providing written informed consent. The control group followed protocolized course classes for 12weeks, while the intervention group integrated two weekly one-hour yoga sessions into their course.

Results: The PAA has approved the implementation of this intervention protocol at Airbase 11 in Beja, highlighting its significance for the organization's policy makers. We hypothesize that this method will enhance operational performance and, subsequently, elevate flight safety.

Discussion: This research's potential extends beyond the PAA, as it can be adapted for use in Airforce departments of other nations and various military contexts.

Clinical trial registration: Évora University research ethics committee—approval number 21050. Study registered on [ClinicalTrials.gov](#) under identifier NCT05821270, registered on April 19, 2023.

KEYWORDS

yoga, airforce pilots, operational performance, military health, aerospace medicine

1 Introduction

Air Force pilots, being healthy adults in a specialized profession, need specific training to maintain optimal performance and safety in the challenging conditions of aviation (1). This profession can negatively affect their performance, physical, and mental well-being, due to:

- Exposure to environmental elements includes factors such as noise, vibration, psychophysiological fatigue, and spatial disorientation (1).
- The evolution of aircraft design has brought about notable improvements in engine performance and aerodynamics, enabling pilots to navigate at elevated altitudes and contend with increased gravitational forces (G-forces). These advancements significantly amplify pilots' psychophysiological responses, especially when combined with the effects of hypoxia, thereby markedly influencing the visual and auditory reaction times of the crew (1, 2).
- Hypoxia stands as the primary hazard during high-altitude flights, leading to increased perceived stress and exertion, elevated heart rate, and reduced functionality of respiratory muscles. Exposure to hypoxia can impair working memory and pattern recognition, posing significant challenges to pilots (3).
- Elevated physiological responses to task-related or cognitive stressors can hinder the ability to navigate and address stressful situations effectively (4).
- Demands of piloting a military aircraft include the efficient operation of the vestibular system to maintain balance within the aircraft cabin (5). Fighter pilots often show a heightened susceptibility to spatial disorientation, which can be attributed to the unique characteristics of the aircraft they pilot. Each aircraft is designed for specific functions, contributing to individual variations in susceptibility (6). An essential attribute of the postural control system is its capacity to devalue unreliable sensory information while prioritizing more dependable inputs—commonly referred to as sensory recalibration. This ability implies that, when confronted with visual impairments, reliance on alternative sensory information systems may be intensified. However, this heightened reliance requires specific training. Targeted balance training has shown promise in significantly improving postural stability by strengthening or recalibrating the remaining sensory systems (7).

Understanding these modern military demands can provide insights for specific training to better prepare pilots and aircrews in countering these threats. Recognizing these factors opens new avenues for training and cognitive preparation (3, 4).

Among various exercise options, incorporating yoga into pilot training is a practical choice for the pilots' demands: its multisensory approach engages compensatory sensory systems in the vestibular system that improve balance, stability, and coordination, while also addressing aspects such as breathing to develop the respiratory system, physical postures to enhance flexibility and strength, embodiment for increased proprioception, and meditation for cognitive preparation (7–11). This method not only addresses the distinctive challenges encountered by pilots but also the expected enhancements in overall well-being and cognitive performance are poised to positively impact

decision-making processes and operational performance during aircraft operations (4).

Yoga encompasses physical, mental, and spiritual practices originating from India. Ashtanga Vinyasa Yoga, known for its substantial movement and complex postures, is a physically demanding style of yoga. It involves interconnected physical postures (asanas), flowing movements (vinyasas), and synchronized breathing techniques (pranayama). Ashtanga emphasizes the harmony of posture, breath control, and gaze. It requires a focus on physical embodiment, coordinating each movement with inhalation or exhalation, which makes it a form of “moving meditation” (8, 9). Various yoga modalities have been shown to have predominantly positive outcomes in different populations (10). The viniyoga principle emphasizes ongoing adaptation for therapeutic benefits, covering poses, conscious breathing, meditation, and philosophy, allowing practitioners to tailor their practice to their health, age, occupation, and lifestyle (11).

In line with this methodology, a specialized yoga practice, AVYSM, tailored for Air Force Pilots has been developed. Understanding the previously mentioned challenges and responsibilities faced by Airforce pilots will be instrumental in guiding the development and evaluation of strategies and training programs, especially:

- establishing the efficacy of AVYSM in refining stress responses in individuals, thus improving cognitive response, and decision-making.
- scrutinizing the impact of AVYSM in stimulating the recalibration of the vestibular system, above all during rotational tasks implying changes in head position in space, to augment postural stability and balance, thereby mitigating spatial disorientation.
- evaluating the extent to which AVYSM contributes to enhanced overall health, body composition, strength, and respiratory performance, serving as a potential countermeasure against hypoxia threats and increased G-forces in the aircraft.

This study aims to determine the suitability of incorporating this method into the training program for Portuguese Air Force pilots, with the goal of enhancing their capabilities and increasing flight safety by preventing human error.

2 Materials and equipment

Material and equipment selection for the study prioritized availability, capability to measure physiological functions impacted by piloting military aircraft, suitability for real-life training integration, and efficiency in delivering results without hindrance to pilots' daily workload, as well as adherence to the highly specific military regulations in force.

Both primary and secondary outcomes were selected following a comprehensive review of the literature and a comparison with pilots' perceived difficulties (as identified through a brief interview, detailed in the study flow). Primary outcomes were deemed the most critical factors in flights, with Operative Performance being the most crucial for pilots' safety. Secondary outcomes were also identified as significant contributors.

2.1 Primary outcomes

Changes in Operative performance—Flight times to complete tasks in the flight simulator; number of errors during the emergency protocol and their classification report from the flight simulator controller (12). The assessment will determine if the exercise protocol influences the pilot's decision-making, as evidenced by improved task efficiency, reduced errors, and enhanced visual and auditory reaction times (1, 2)—Time Frame: measured at 12 weeks (vs. baseline values).

Changes in Stress and HRV—Heart rate variability, measured with Polar H10 portable device (2, 13–15). The assessment will reveal if the exercise protocol influences pilots' responses to stressors, with a lower stress response enhancing decision-making (4)—Time Frame: measured at 12 weeks (vs. baseline values).

Changes in Vestibular system control responses—The Center of Pressure (CoP) represents the dynamics of the neuromusculoskeletal system, was measured with a portable force plate (Biosignals Plux-Portugal) with a sample frequency at 1000 Hz and data downsampled to 100 Hz (16, 17). Preprocessing performed using the EEGLAB toolbox, which is available for use in MATLAB (The MathWorks Inc., Natick, MA) (18). Enhanced postural control responses may indicate the protocol's potential to mitigate the effects of spatial disorientation (6, 7)—Time Frame: measured at 12 weeks (vs. baseline values).

2.2 Secondary outcomes

Changes in Strength—Handgrip strength measured with a handgrip dynamometer Baseline Smedley, Model 12–0286, White Plains, NY, United States (19). The assessment will determine if the exercise protocol impacts pilot strength, crucial for maintaining control, resisting fatigue, and ensuring safety during high-intensity flights (2)—Time Frame: measured at 12 weeks (vs. baseline values).

Changes in Body composition—Body composition data (percent body fat, percent fat free mass, percent muscle mass index, as a percentages) measured with a Tanita (MC-780 MA, Tanita, Tokyo, Japan) to get a bioelectrical impedance analysis (BIA) will indicate if the exercise protocol had any impact in the pilot's physical makeup. Percent body fat, percent fat-free mass, and percent muscle mass index collectively constitute body composition measures. Percent body fat reflects the fat proportion in total body weight, encompassing essential and storage fat. In contrast, percent fat-free mass represents the non-fat components, including muscle, bone, organs, and other tissues. Percent muscle mass index specifically gauges the proportion of body weight attributed to muscle. The relationship between percent body fat and percent fat-free mass is complementary, totaling 100%, while percent muscle mass index indicates the proportion of muscle within total body weight (20, 21). Enhanced body composition could mitigate adverse effects of the pilot profession on physical well-being (1)—Time Frame: measured at 12 weeks (vs. baseline values).

Changes in well-being and general health—measured through the SF-36 V1 questionnaire (22, 23) will indicate if the exercise protocol had any impact in the pilot's general health subjective assessment, mitigating adverse effects of their profession on pilots' physical well-being (1)—Time Frame: measured at 12 weeks (vs. baseline values).

Changes in Lung capacity—Ventilatory response measured with spirometry—FEV1/FVC (Forced Expiratory Volume in 1 s and Forced Vital Capacity) ratio indicates how much air you can forcefully exhale

(2, 5) will indicate if the exercise protocol had any impact on lung capacity, which might offset hypoxia threats on pilots (3) – Time Frame: measured at 12 weeks (vs. baseline values).

Five Facet Mindfulness Questionnaire (FFMQ)—Changes in cognitive abilities with 15 questions and average scores are calculated by summing the responses and dividing by the number of items, and indicate the average level of agreement with each subscale (1 = rarely true, 5 = always true). Higher scores are indicative of someone who is more mindful in their everyday life (24, 25). Determining the impact of the exercise protocol on cognitive abilities, a more mindful pilot is anticipated to exhibit improved decision-making skills during work (1, 3)—Time Frame: measured at 12 weeks (vs. baseline values).

Multidimensional Assessment of Interoceptive Awareness Questionnaire (MAIA)—Changes in cognitive abilities—is an 8-scale state-trait questionnaire with 32 items to measure multiple dimensions of interoception; scores are between 0 and 5, where higher score equates to more awareness of bodily sensation (26). The evaluation will assess the exercise protocol's impact on cognitive abilities, expecting improved decision-making in pilots with heightened awareness of bodily sensations (1, 3)—Time Frame: measured at 12 weeks (vs. baseline values).

Aviation Safety Attitude Scale (ASAS)—Changes in cognitive abilities—consists of 27 items on a five-point scale, each designed specifically to assess pilots' attitudes with respect to predict the hazardous event involvement of aviators; For all the attitude subscales, higher scores indicate a greater degree of that particular attitude—For example, higher scores on the ASAS self-confidence factor indicated that the person expressed greater confidence in their ability as a pilot (27). The evaluation will assess the exercise protocol's impact on cognitive abilities, anticipating enhanced decision-making skills in more confident pilots (1, 3)—Time Frame: measured at 12 weeks (vs. baseline values).

3 Methods

3.1 Study design, ethics approval and informed consent publication

The study was approved by the Évora University Research Ethics Committee, with approval number 21050, and participants gave written informed consent. The study is in agreement with the Declaration of Helsinki. The trial was registered in [ClinicalTrials.gov](https://clinicaltrials.gov) with identifier NCT05821270, registered on 19th April 2023. Furthermore, this intervention protocol was accepted by the PAto be applied on Airbase 11 in Beja. A randomized, prospective, controlled two-arm trial will be adopted, in which one arm will be the control group (waiting list) and the other the intervention group (yoga).

3.2 Participants

3.2.1 Sample size determination

Among all military personnel in the Portuguese Air Force, the inclusion criteria for participation in this study comprise healthy individuals serving as military pilots actively engaged in their training (tirocinium) at the PAA, which consists of taking the course titled “Masters in Military Aeronautics: Aviator Pilot Specialist.”

Conversely, the exclusion criteria encompass military pilots on active duty either preceding (not aviation pilots yet) or following the tirocinium (distributed by different airbases inside and outside the country and flying different types of aircrafts in restricted, classified or warzones), those with injuries, and individuals undergoing sudden lifestyle changes (e.g., initiating or discontinuing smoking habits, commencing, or ceasing any form of medication, or adopting a new diet).

There are currently 19 pilots actively undergoing their training (tirocinium) at the PAA, serving within “Esquadra 101 - RONCOS,” situated at Airbase 11 in Beja, which comprises the totality of this population for the PA. These pilots are divided into two classes, and they share common aircrafts, specifically the Aerospacia Epsilon TB-30. Additionally, both classes are assigned comparable workloads and operational tasks.

Within these criteria there are 19 individuals serving as military pilots actively engaged in their training (tirocinium) at the PAA, specifically within the PA course titled “Masters in Military Aeronautics: Aviator Pilot Specialist,” and our sample size is calculated with OpenEpi, with a 95% confidence interval, which corresponds to 19 subjects—the totality of this population, as seen in [Image 1](#).

3.2.2 Recruitment and screening

The collaboration between Évora University and the PA involved reaching out to the Head of the Chief of Staff Cabinet. Under this collaborative protocol, a Ph.D. student will administer a yoga intervention at the chosen airbase 11 in Beja, while a team from Évora University conducts on-site baseline and post-intervention data

collection. The authorization for this collaborative effort was granted by the Portuguese Air Force’s Head of the Chief of Staff Cabinet.

Pilots will undergo a comprehensive briefing on the study’s general parameters and will be extended a voluntary invitation to participate. Following this briefing, participants will be required to sign an informed consent form in adherence to the Helsinki Declaration. Any queries or concerns can be addressed during this stage to ensure clarity and compliance with ethical standards.

3.2.3 Randomization procedure and blinding

Upon inclusion, volunteers will be allocated to either a waiting list (control group) or a yoga class (intervention group) through a computer-based algorithm ([random.org](#)), to be facilitated by the team captain of the pilots. All study personnel, excluding the team captain and one study coordinator from Évora University, will be kept unaware of the group allocation. Participants will be explicitly instructed to refrain from disclosing their group assignment to the study team. To uphold impartiality, all data will be coded for subsequent processing and analysis, maintaining blindness to group allocation. The final coded trial dataset will be made available to all team members for analysis.

3.3 Experimental procedure

3.3.1 Study flow

The study team will visit Airbase 5 in Monte Real to consult with the F16 Team Captain. The objectives include planning and scheduling

Sample Size for Frequency in a Population

Population size(for finite population correction factor or fpc)(N): 19

Hypothesized % frequency of outcome factor in the population (p):50%+/-5

Confidence limits as % of 100(absolute +/- %)(d): 5%

Design effect (for cluster surveys-DEFF): 1

Sample Size(n) for Various Confidence Levels

ConfidenceLevel(%)	Sample Size
95%	19
80%	18
90%	18
97%	19
99%	19
99.9%	19
99.99%	19

Equation

Sample size $n = [DEFF * Np(1-p)] / [(d^2 / Z^2_{1-\alpha/2} * (N-1) + p * (1-p))]$

Results from OpenEpi, Version 3, open source calculator--SSPropor

Print from the browser with ctrl-P

or select text to copy and paste to other programs.

IMAGE 1

Sample size for frequency in the military pilot's population using OpenEpi.

visits, testing the proposed protocol, assessing all pertinent equipment, identifying, and rectifying potential errors before the initiation of the initial data collection. During this meeting, interviews with the Team Captain will be conducted to evaluate the perceived needs of pilots during their aircraft piloting duties. The insights obtained, combined with findings from the literature, will guide the tailoring of the yoga intervention.

A baseline data collection session will be organized in Airbase 11 in Beja, with study participants selected randomly based on availability and location undergoing evaluation over two consecutive days during pilots’ work hours from 8:30 to 19:00. Oversight of the data collection will be provided by experts in Sports Exercise and Health from Évora University, the study coordinator, and a simulator controller from the Air Force team.

The yoga group will integrate a one-hour yoga class into their work schedule, in Airbase 11 in Beja, twice a week for a 12-week period. For those on missions with conflicting schedules, alternative days and times will be accommodated. Each pilot is required to complete 24 yoga classes within the designated 12 weeks. The yoga intervention, led by the study coordinator—an Ashtanga Vinyasa Yoga expert with over 300 h of training and approximately 10 years of teaching experience—will be conducted.

Post-intervention data collection will follow the completion of the yoga program, with study participants, randomly divided based on availability and location, undergoing evaluation over two consecutive days, in Airbase 11 in Beja, during pilots’ work hours from 8:30 to 19:00. Supervision will be provided by experts in Sports Exercise and Health from Évora University, the study coordinator, and an available simulator controller from the Air Force team.

Upon the study’s conclusion, the waiting list group will be offered the same 12-week yoga classes before completing their tirocinium and departing the airbase, aligning with ethical considerations.

3.3.2 Practical applicability

The communication strategy for disseminating trial results to participants and Air Force professionals involves presenting comprehensive data collection information, results, and conclusions to the Health and Exercise Department of the Portuguese Air Force. This initiative holds particular significance as there is currently no established formal exercise program for training aircraft pilots. The outcomes of this study may prove instrumental in the creation or enhancement of such a program, thereby contributing to the improvement of future military health policy.

For the broader public and other pertinent groups, access to the study’s findings can be facilitated through publication in scientific journals. This dissemination approach ensures that the study’s outcomes are accessible to a wider audience, contributing to the broader scientific and professional knowledge base.

3.3.3 Arms and intervention

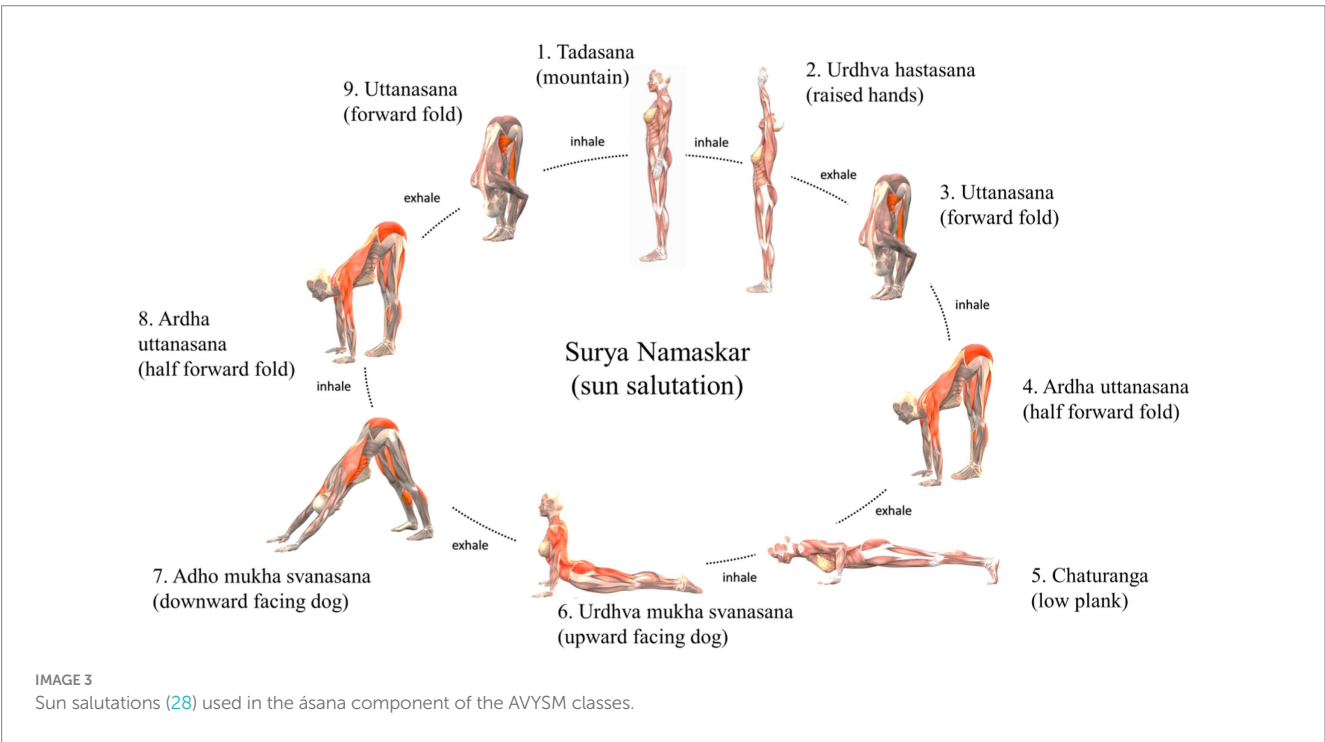
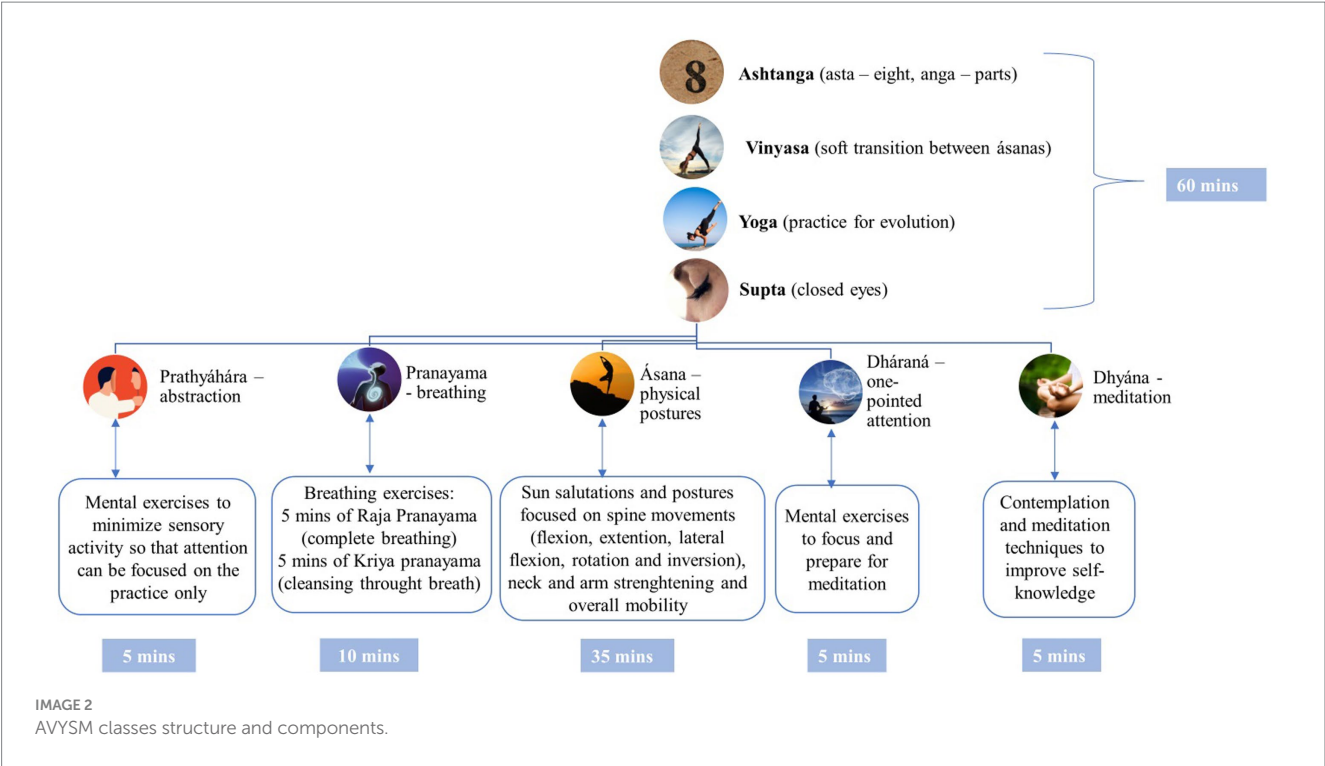
Table 1 outlines the study arms: the control group receiving military training alone and the intervention group undergoing both military training and yoga classes.

The yoga practice, as depicted in Image 2, entails fluid sequences (Ashtanga Vinyasa Yoga) performed with closed eyes (supta) to address perceived difficulties in pilots. The yoga classes comprise five main components:

TABLE 1 Arms and assigned interventions of the study protocol.

Arms	Assigned interventions
Experimental: Yoga	Yoga practice: 12-week program of Ashtanga Vinyasa Yoga Supta for 1 h twice a week; other names – yoga class
No Intervention: Waiting list	Exclusively compulsory training (the same for all academy attendees).

- 5 min of prathyāhara (abstraction)—“withdrawal of the senses” or “sensory withdrawal,” involves consciously detaching the senses from external stimuli and directing attention inward. Through pratyahara, practitioners aim to disengage from external distractions, facilitating a deeper exploration of the inner self and enhancing self-awareness.
- 5 min of pranayama (breathwork, including raja pranayama and kryia)—these are advanced forms of breathwork aimed at regulating the breath and influencing the flow of prana (life force energy) throughout the body. Raja Pranayama focuses on controlling the breath through various breath retention methods, such as inhaling (puraka), holding the breath (kumbhaka), and exhaling (rechaka) in specific ratios. Kriya pranayama techniques typically combine specific breath control, body postures, and mental focus to influence the flow of prana (life force energy) throughout the body. Nauli Kriya is an advanced yogic purification technique that involves isolating and rhythmically churning the abdominal muscles. It is performed by contracting and rolling the abdominal muscles in a specific manner to create a rolling or rippling motion across the abdomen.
- 35 min of āsana (physical postures)—with sun salutations, as depicted in Image 3 and sequenced physical postures, as depicted in Image 4, involving spinal flexion, extension, lateral flexion, rotation, and inversions, changes in head positioning entailing a recalibration involving the integration of visual, vestibular, and muscular sensations, combined with breath control and abstraction, for a holistic approach to health and well-being.
- 5 min of dhāraṇā (practice of concentration or single-pointed focus)—beginning with yoga nidra for physiological relaxation, followed by mental exercises to focus and prepare for meditation. Yoga nidra is the practice of deep relaxation or yogic sleep. It is a state of consciousness between wakefulness and sleep, where the body and mind are in a state of profound rest while remaining fully aware. During yoga nidra, practitioners typically lie down in a comfortable position and follow guided instructions to systematically relax different parts of the body, release tension, and enter a state of deep relaxation. The practice often involves techniques such as body scanning, breath awareness, visualization, and mindfulness. Dhāraṇā involves directing one’s attention to a specific object, thought, or sensation, and maintaining that focus without distraction. This object of focus could be anything, such as a physical object, a mental image, a mantra, or the breath. The goal of dhāraṇā is to develop greater mental discipline, control over the wandering mind, and the ability to sustain attention for prolonged periods.
- 5 min of dhyāna (meditation or contemplation)—involves focused concentration and sustained attention on an object, thought, or sensation to achieve a state of mental clarity, stillness, and inner awareness. During dhyana, practitioners aim to quiet



the mind, transcend distractions, and cultivate a deep sense of presence and mindfulness, focused on developing greater mental resilience and emotional balance. Sankalpa (“resolve” or “intention”) was also used during meditation, it is a tool used to set a clear and positive intention for one’s life or practice, a heartfelt affirmation of one’s deepest values, aspirations, and purpose. It serves as a constant reminder of what truly matters

and empowers individuals to align their thoughts, words, and deeds with their deepest intentions.

The components will be adapted to the specific needs of the pilot group during their flight missions: supta classes, primarily or entirely conducted with closed eyes, aim to eliminate visual system responses and evoke vestibular system responses; Ashtanga



IMAGE 4

Various yoga postures (āsanas) incorporated in the āsana component of the AVYSM classes.

Vinyasa classes emphasize fluid movement sequences, focusing on breathing and enhancing neck and upper limb strength through various yogic movements available to the head and spine (flexion, extension, lateral flexion, rotation, and inversion). This recalibration facilitates the pilot's awareness of their spatial orientation, complemented by improvements in embodiment and proprioception. This, in turn, enhances the pilot's perception of the aircraft's orientation and their own position in relation to it, as well as their spatial awareness of the aircraft in relation to the Earth. The classes will commence with basic-level techniques, progressing to more advanced ones as the intervention group's proficiency and abilities improve over the timeline.

3.3.4 Statistical analysis

Sample size was calculated with OpenEpi. Data analyses will be done with MATLAB (18) and Jamovi (29), based on the type of data; analyses will be performed based on the underlying assumptions for parametric, or non-parametric testing. In detail, for all difference testing, data and variance distribution (i.e., normality) will be checked. The alpha-error threshold is set at 5%, all p values below are considered significant.

For the primary outcomes related with postural control and heart rate variability a MATLAB (18) routine will be used to treat data exported from the Biosignals Plux platform and also from the Polar H10 portable monitor, and with those values a Shapiro–Wilk normality test will be performed and either a T-test for paired samples will be applied on parametric data or a Wilcoxon rank test will be applied on non-parametric data.

For the primary outcomes related with operative performance and the secondary outcomes a Shapiro–Wilk normality test will be performed

and either a T-test for paired samples will be applied on parametric data or a Wilcoxon rank test will be applied on non-parametric data.

4 Results

The principal objective of the study is to assess the feasibility and efficacy of implementing a 12-week yoga program to enhance existing military training protocols within the Portuguese Air Force. This will be accomplished through the utilization of a randomized controlled intervention design. The intervention comprises preventive exercises tailored to address perceived challenges faced by pilots during aircraft piloting, thereby enhancing the capabilities of individuals who are already undergoing training.

The findings of this study hold significance for the research group and are equally pertinent for policymakers within the Portuguese Air Force. The data gathered in this project can aid policy makers in developing a tailored exercise regimen.

Broadening the study's relevance to diverse contexts, the methods, results, and discussions generated by this project have the potential to be extrapolated to diverse military contexts, beyond military aviation, exploring applications of human intervention in different military settings, such as incorporating new training techniques for: airfield operations officers, paratroopers, armored vehicle operators, tank crews, navy divers, military paratroopers, and others, where the improvement of physical and cognitive abilities aligns with the outcomes of this study. Furthermore, the applicability of the project's findings extends to high-demand environments beyond military, including civil aviation (both for pilots and air traffic controllers), professional race car or motorcycle drivers and skydiving

companies—professions where the optimization of physical and cognitive capabilities may offer valuable insights and benefits.

5 Discussion

Recognizing the critical role of cognitive performance in military operations, where impaired cognitive function is a prominent factor in accidents during training and combat (30), instructors must prioritize not only the physical health but also the psychological well-being of trainee pilots (31). The potential to enhance sensory systems, particularly through vestibular habituation and adaptation, can influence sensory weighting and postural behavior, the processing of sensations, along with their identification and integration with others, providing a comprehensive framework of possibilities for decision-making and action planning (32). Consistent yoga practice contributes to ongoing improvement in postural control, muscle strength, and the vestibular system, fostering increased plasticity in the sacculocolic pathway and resulting in enhanced vestibular evoked myogenic potential (cVEMP) responses (32). Furthermore, Ashtanga Yoga, in accordance with Patanjali, encompasses techniques that address all facets of the human system, including the body, breath, mind, personality, and emotions (11).

A notable strength of this intervention lies in its practicality and cost-effectiveness. Furthermore, all exercises are executable without the need for additional materials and can be conducted in spaces already designated for training, such as a gym room or outdoors when weather conditions permit.

The sample size may present challenges in interpreting results and deducing the practical relevance of the study. Challenges in maintaining blinding among pilots also present potential limitations. These are mitigated by including the totality of this population, designating the control group as a waiting list, offering them the same intervention subsequently, and ensuring blinding for all investigators except the study coordinator.

As civilians, we secured explicit authorization to conduct this study within a military setting. Compliance with specific military regulations, legal constraints, and adherence to classified information protocols were paramount. Notably, due to operational constraints, especially in classified, restricted or warzone areas, the team could only study and publish information from active pilots taking their Tirolcinium. The team was able to study the pilots while they worked, gaining hands-on experience and practical skills before assuming their full duties. Testing moments had to synchronize with the pilots' professional commitments and occur in non-classified areas. The study focused solely on Tirolcinium Pilots, given the limitations in examining Airforce Pilots. These measures ensured alignment with legal, security, and operational considerations during the study.

Currently, the Portuguese Air Force's Health and Exercise Department lacks an official exercise training program for pilots. Pilots are generally instructed to train in a manner they deem suitable to meet mandatory physical testing requirements. Information obtained from this study holds potential utility in the development of a structured training program and the adaptation of physical evaluation tools, thereby improving future military health policy and legislation. This research's potential extends beyond the PA, as it can be adapted for use in Airforce departments of other nations and various military or high-performance contexts.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Évora University research ethics committee—approval number 21050. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

SS: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Software, Writing – original draft. FM: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. OF: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. JP: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The mechanisms linking perceived stress to pilots' safety attitudes: a chain mediation effect of job burnout and cognitive flexibility

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Introduction: Pilots' safety attitude is crucial for aviation safety. Current research shows a correlation between perceived stress and safety attitude, yet the mechanism underlying this association remains unclear. Against the backdrop of heightened attention to pilots' stress, this study aims to thoroughly explore the inherent connection between pilot safety attitudes and their perceived stress, offering targeted insights into preventing and addressing safety attitude issues arising from pilot stress.

Methods: Through path analysis of questionnaire data from 106 civil aviation pilots in China, this study systematically investigates the roles of job burnout and cognitive flexibility in the relationship between perceived stress and safety attitude. The study reveals the chain-mediated mechanism of these two factors.

Results: The results demonstrate a significantly negative correlation between pilots' perceived stress and safety attitude, with cognitive flexibility and job burnout fully mediating this relationship, and cognitive flexibility affecting job burnout. A detailed analysis of the three dimensions of job burnout reveals varying impacts of emotional exhaustion, depersonalization, and reduced personal accomplishment on the aforementioned path. The research model exhibits a good fit (GFI=0.902), providing new theoretical perspectives on the association between pilots' perceived stress and safety attitude.

Discussion: The findings offer practical implications for improving pilots' safety attitude by proposing targeted measures to alleviate the adverse impacts of perceived stress on safety attitude, thereby promoting aviation safety.

KEYWORDS

perceived stress, safety attitudes, job burnout, cognitive flexibility, pilots, mediation effect

Highlights

- **Innovative Perspectives & Holistic Exploration:** This study unveils that the relationship between pilots' perceived stress and safety attitudes is not a straightforward causal link but rather intricately influenced by other variables. Approaching the issue through the lenses of job burnout and cognitive flexibility, our research systematically investigates the roles of these factors in the nexus between perceived stress and safety attitudes. This provides a novel theoretical perspective, expanding our comprehension of the mechanisms shaping pilots' psychological well-being and safety attitudes.
- **Empirical Validation of Amplification Effects:** By delineating the three dimensions of job burnout, our research empirically substantiates the transmission and amplification effects of stress. Quantifying the inherent logic in the connections among perceived stress, cognitive flexibility, job burnout, and safety attitudes contributes to advancing the corresponding theories.
- **Practical Insights for Augmented Safety:** Proposing the mediating roles of job burnout and cognitive flexibility offers practical insights for enhancing pilot safety attitudes. Recommendations for airlines include strengthening organizational support, improving working conditions, providing positive feedback, and conducting cognitive training programs to alleviate the impact of perceived stress on safety attitudes.

1 Introduction

In the aviation industry, flight safety stands as a paramount concern. One central to this is the safety attitudes of pilots, which encompass their beliefs about safety's importance and their motivation to act upon these beliefs (1). Previous studies have underscored the pivotal role of these attitudes in shaping pilots' risk perception, prioritizing safety during emergencies, and influencing decision-making (2). Negative safety attitudes were pinpointed as key contributors to aviation accidents and precursor events (3). Conversely, positive safety attitudes bolster pilots' professional pride and standardize safety procedures, leading to a decrease in unsafe behaviors and the likelihood of accidents (4, 5).

Given that attitudes significantly shape behavior, understanding these underlying beliefs is essential when aiming to drive behavioral change (6). However, current research has yet to delve into the factors shaping pilots' safety attitudes, leaving a critical knowledge gap that hampers effective strategies for enhancing flight safety.

To bridge this gap, this study seeks to elucidate the pathways influencing pilot safety attitudes, offering both theoretical and empirical foundations for designing more impactful safety training and educational programs. By conducting a comprehensive literature review, empirical investigations, and quantitative data analysis, this study aims to uncover the mechanisms that shape these attitudes. These findings aspire to introduce fresh perspectives and methodologies to aviation safety management, with a specific focus on reducing accidents through the enhancement of pilots' safety attitudes. This study holds significant implications for airlines, safety management professionals, and policymakers striving to elevate safety standards within the aviation industry.

1.1 Relationship between perceived stress and safety attitude

Stress encompasses the various demands and expectations individuals encounter in their work, accompanied by corresponding psychological and physiological responses (7). As a subjective experience, perceived stress can vary widely among individuals exposed to the same work environment and job requirements. Within the pilot profession, stress emerges as a pervasive factor influenced by diverse elements such as family issues, social stressors, career uncertainties, aircraft accidents, and demanding flight schedules. While moderate levels of stress can help maintain pilots' focus, excessive stress can impair performance. When the underlying causes of perceived stress remain unaddressed, stress tends to accumulate, leading to persistent and escalating levels. This chronic stress can detrimentally affect commercial pilots both physiologically and psychologically, significantly compromising their flying capabilities (8).

Research has shown that pilots who fail to cope with stress may become depressed or even self-destructive. They may externalize their feelings and show them, or blame their misfortunes on others. When pilots encounter unexpected situations, those who perceive high levels of stress may exhibit "warning signals," such as defensiveness, arrogance, hostility, deterioration in pilot performance, or increased risk-taking (9). Other studies have also revealed a negative correlation between pilots' perceived stress and their safety attitudes through quantitative data (10–12).

However, despite existing research on the correlation between a pilot's safety attitude and their perceived stress, the relationship between perceived stress and safety attitude is not a straightforward cause-and-effect scenario. In this process, the influence of buffering variables remains unexplored, and the specific psychological mechanisms through which pilot stress affects their safety attitude have yet to be elucidated.

Research has demonstrated that higher stress levels are perceived by pilots in comparison to individuals engaged in alternative occupations (13). To effectively mitigate the risks of aviation accidents stemming from safety attitudes, it is crucial to delve into the path relationship between a pilot's perceived stress and their safety attitude, examining the impact pathways and mechanisms through which stress influences safety attitudes and identifying key mediating variables. This comprehensive exploration is not only beneficial for unveiling the psychological processes through which stress affects safety attitudes but also provides a basis for aviation companies and training institutions.

Building upon this, the first hypothesis proposed in this study is as follows:

H1: There is a significant negative correlation between a pilot's perceived stress and their safety attitude.

1.2 Mediating role of job burnout

The concept of job burnout was initially introduced by Freudenberg in psychology to describe a state of overwhelming exhaustion when work excessively demands an individual's

capabilities, energy, and resources (14). It was subsequently divided into three dimensions by Maslach and Jackson: emotional exhaustion, depersonalization, and reduced personal accomplishment (15).

Compared to individuals with low levels of job burnout, those with high levels are more susceptible to the spiral of resource depletion and are observed to conserve their limited energy to avoid further resource loss (16, 17). According to the Conservation of Resources theory, individuals are believed to possess finite personal resources and, driven by an innate self-protective instinct, are driven to acquire, preserve, and maintain these resources. A continuous drain on their emotional and mental resources is acutely felt by individuals experiencing high levels of job burnout, particularly when they perceive a deficit in personal resources, which may lead them to refrain from investing additional resources in maintaining safety, thereby leading to non-compliance with safety regulations, neglect of safety procedures, and disregard for safety risks.

Furthermore, the Job Demand-Resource theory (18), along with quantitative studies on employees (19) and nurses (20), has indicated that stressors such as work overload, lack of autonomy, emotional demands, low social support, and role ambiguity can result in feelings of exhaustion and the development of negative, callous attitudes toward work (21). When the work demands perceived surpass the available resources, heightened levels of perceived stress are experienced by individuals, who not only confront the challenges of their job but also grapple with additional psychological burdens. As a result, these individuals are more prone to fatigue and resource depletion, culminating in job burnout (22, 23).

For pilots, increased perceived stress and work demands can lead to the onset of job burnout. Recognizing signs of burnout, pilots may become more sensitive to resource depletion. Thus, when pilots are engaged in activities that consume more of their precious physical and cognitive resources, such as implementing spontaneous safety changes and safety suggestions while striving to complete flight tasks (24), they are more inclined to adopt a passive safety attitude of neglecting or avoiding safety behaviors, including reducing work enthusiasm and lowering work engagement, among other things.

Hence, this study proposes the hypotheses:

H2a: Pilots' job burnout is positively correlated with their safety attitudes.

H2b: Pilots' job burnout plays a mediating role in the relationship between their perceived stress and safety attitudes.

1.3 Mediating role of cognitive flexibility

Cognitive flexibility, a core component of executive function, plays a pivotal role in enabling individuals to swiftly adjust and adapt cognitive strategies when confronted with new information or environments (25). This capability allows individuals to transition between different cognitive states, facilitating adept navigation of complex and ever-changing situations (26). Given that pilots require not only proficient flying skills but also the ability to make informed decisions based on specific contexts and maintain situational

awareness, cognitive flexibility emerges as a highly prized attribute among pilots (27, 28).

Research has indicated that individuals with high cognitive flexibility exhibit proactive thinking, suggesting multiple solutions when facing intricate challenges rather than avoiding them (29). This proactive approach correlates with enhanced adaptability and superior coping strategies (30). Moreover, individuals with high cognitive flexibility typically demonstrate stronger social and cognitive abilities, fostering more effective communication and collaboration with peers. In contrast, those with low cognitive flexibility often display diminished social interaction skills and cognitive proficiency (31). For instance, a study involving emergency service personnel revealed that individuals with high cognitive flexibility remain mentally agile and alert, capturing diverse cues in their environment. This heightened awareness correlates with elevated safety attitudes and situational awareness, effectively mitigating unsafe behaviors and conspicuous operational errors (32).

Furthermore, cognitive flexibility has been observed to be influenced by perceived stress (33). High-stress environments pose challenges for individuals in task-switching and adapting to new circumstances, primarily due to stress-induced impairment of key prefrontal cortex regions responsible for executive functions like working memory and attention (34, 35). Studies on nursing populations have also corroborated a negative correlation between stress levels and cognitive flexibility (36), suggesting that higher stress levels are associated with decreased cognitive flexibility.

Given the aforementioned findings, it can be surmised that perceived stress may impact pilots' safety attitudes through the mediating effect of cognitive flexibility. Elevated perceived stress levels could impair cognitive flexibility, hindering pilots' ability to swiftly adapt cognitive strategies when faced with complex and novel flight situations. This compromised cognitive flexibility may diminish pilots' alertness and coping capabilities, potentially resulting in decision-making errors or unsafe behaviors during operations.

Based on this, the study proposes the following hypotheses:

H3a: Pilot cognitive flexibility is positively correlated with their safety attitudes.

H3b: Pilot cognitive flexibility plays a mediating role in the relationship between their perceived stress and safety attitudes.

1.4 Chain-mediation role of flexibility and job burnout

Cognitive flexibility refers to an individual's ability to process information, adapt to changes, and solve problems. It entails the capability to quickly and effectively adjust cognitive strategies across various tasks and environments. Job burnout, on the other hand, is characterized by physical and mental exhaustion stemming from prolonged work pressure and psychological strain, potentially resulting in diminished interest and enthusiasm toward work.

According to behavioral regulation theory, individuals engage in goal-oriented behavior through a series of cognitive processes, encompassing goal setting, selection, internal and external orientation,

planning, execution monitoring, and feedback processing. A decline in cognitive flexibility can pose several challenges for individuals. Firstly, it may hinder their ability to set clear work goals or select appropriate ones, thereby affecting planning and execution monitoring. Secondly, individuals may struggle to process work feedback and find it challenging to adapt their behavior accordingly. Consequently, reduced cognitive flexibility can render work objectives ambiguous, leading to diminished motivation and direction in work tasks. This situation can contribute to the onset of job burnout, making it difficult for individuals to cope effectively with work challenges (37). Empirical research corroborated this perspective, revealing a correlation between job burnout and impaired executive function (38). This suggests that prolonged occupational stress may compromise cognitive function, subsequently influencing individual job burnout and safety attitudes.

When pilots confront high levels of work pressure and challenges, their cognitive abilities may suffer, resulting in reduced efficiency in executing control and difficulties in organizing and regulating their actions effectively. As a result, diminished cognitive flexibility can make pilots more vulnerable to feeling overwhelmed and experiencing job burnout. This can lead them to overlook safety considerations and develop negative safety attitudes.

Therefore, this study proposes the following hypothesis:

H4: Cognitive flexibility and job burnout play a chain-mediated role in the relationship between perceived stress and safety attitudes.

2 Methods

2.1 Participants

This research focuses on conducting a survey study among Chinese civil aviation pilots, employing a random sampling approach. Researchers initially developed the research questionnaire as an online electronic survey and generated a QR code for distribution. The questionnaire included variable questions mentioned in the literature review section as well as demographic questions. Between September 21, 2023, and November 1, 2023, researchers randomly selected a class of pilots undergoing recurrent training and presented the QR code to invite pilots to participate anonymously in the survey. A total of 137 pilot responses were collected for this study, of which 106 pilot data were analyzed after the removal of outliers. It is noteworthy that all participants in this survey were male, consistent with the disproportionately low representation of female pilots in the Chinese civil aviation industry (39). Ethical approval for this research was obtained from the Ethics Committee of the author's institution, and all procedures were conducted by relevant guidelines and regulations.

Table 1 presents the basic demographic information of the participants. The data collection showed a nearly 2:1 ratio between First officers and captains/instructors, aligning with the typical distribution of pilots in China. This suggests that the collected data to some extent represents the Chinese pilot population. Additionally, the data predominantly falls within the 21–40 age range, with an average age of 33.593 ± 7.702 years. The distribution of flight experience aligns with the distribution of professional titles among pilots.

TABLE 1 Demographics of participants ($n = 106$).

	Group	N	%
Post	First Officer	59	55.7
	Captain	25	23.6
	Instructor	22	20.8
Age	21–30	49	46.2
	31–40	41	38.7
	40+	16	15.1
Flight experience	0–3,000	44	41.5
	3,001–7,000	26	24.5
	7,000+	36	34.0
Total		106	100

2.2 Self-reported scales

2.2.1 Pilot safety attitude questionnaire

Pilot safety attitudes are reflected in their performance in training, and work, as well as in communication and collaboration with other pilots. Based on a literature review (40) and in-depth interviews with flight management personnel from a certain airline, this study modified the safety attitude evaluation indicator system of the airline. After removing inappropriate questions, five items were retained to measure pilots' safety attitudes. These items are as follows: (1) In daily operations, I voluntarily report safety hazards; (2) In daily operations, I actively provide safety suggestions to the company; (3) In daily operations, I frequently communicate safety information with others; (4) In daily operations, I actively learn flight-related knowledge from various sources; (5) In training, I proactively identify and address weaknesses in my skills for training and improvement. The 5-point Likert scoring method was used in the questionnaire. The higher the score, the better the safety attitude. The Cronbach's alpha for this measurement was 0.809, indicating a high level of internal consistency. For the validity analysis of the questionnaire, based on the single-factor structure analysis, the factor loadings for all items were greater than 0.4. The KMO value was 0.745, and the p -value in Bartlett's test of sphericity was 0.000.

2.2.2 Perceived stress questionnaire

In a stress study specific to civil aviation pilots, which integrates the OSI (Occupational Stress Inventory) occupational stress measurement indicator system, the sources of pilots' perceived stress were categorized as the job itself, career development, interpersonal relationships, work–family conflict, and organizational factors (7). The questionnaire utilized a five-point scale for self-assessment, where scores from 1 to 5 represent the degree of conformity from “completely inconsistent” to “completely consistent.” Higher scores indicate greater perceived stress, while lower scores suggest lower perceived stress. For the reliability and validity analysis of the questionnaire, all questions were combined into one dimension. The overall reliability of Cronbach's alpha was 0.956. Additionally, the factor loadings for all items on each dimension were greater than 0.4. The KMO value was 0.852, and the p -value in Bartlett's test of sphericity was 0.000.

2.2.3 Job burnout questionnaire

Maslach's three-dimensional model defines burnout as a psychological syndrome resulting from the job itself, encompassing the dimensions of emotional exhaustion, depersonalization, and reduced personal accomplishment. The MBI-GS scale is provided as a quantitative measurement tool. This study adheres to the 7-point self-assessment format employed by the scale, with scores ranging from 1 to 7. A score of 1 represents "never," 2 corresponds to "a few times or less per year," 3 to "once a month or less," 4 to "a few times a month," 5 to "once a week," 6 to "a few times a week," and 7 to "every day." Higher scores indicate stronger burnout. The Cronbach's alpha for each sub-dimension in this questionnaire was 0.948, 0.836, and 0.803, with a total Cronbach's alpha of 0.903. For the validity analysis of the questionnaire, the KMO values for each dimension were 0.900, 0.740, and 0.796, and the *p*-values in Bartlett's test of sphericity were all 0.000.

2.2.4 Cognitive flexibility questionnaire

Cognitive flexibility refers to an individual's ability to freely change their cognitive approach in different situations, adapting to environmental changes and demands. Martin & Rubin developed the Cognitive Flexibility Inventory (CFI) to assess the flexibility of an individual's cognitive adaptation. The scale employs a 5-point self-assessment format, with 1 indicating "strongly disagree" and 5 indicating "strongly agree." Higher scores reflect greater cognitive flexibility. The Cronbach's alpha for the measurement in this questionnaire was 0.794. For the validity analysis of the questionnaire, based on the single-factor structure analysis, the factor loadings for all items were greater than 0.4. The KMO value was 0.851, and the *p*-value in Bartlett's test of sphericity was 0.000.

2.3 Model hypothesis

As shown in Figure 1, based on the hypotheses from the literature review, the mathematical expressions of the main models in this study were summarized as follows.

$$\text{Safety attitude} = b_1 * \text{Job burnout} + b_2 * \text{Cognitive flexibility} + c * \text{Perceived stress} + e_1$$

$$\text{Job burnout} = a_1 * \text{Perceived stress} + d * \text{Cognitive flexibility} + e_2$$

$$\text{Cognitive flexibility} = a_2 * \text{Perceived stress} + e_3$$

2.4 Data processing

To mitigate the potential issue of common method bias, the present study initially employed Harman's single-factor test for the detection of common method bias. Subsequently, this research utilized correlation analysis to discern the relationships among various factors as mentioned in the literature review section, while also examining the presence of multicollinearity issues. Following this, stepwise regression analysis was employed to ascertain the existence and direction of the effects of different variables on pilots' safety attitudes. Finally, path analysis was conducted to explore the intricate relationships among variables, aiming to gain a deeper understanding of the mechanism underlying the formation of safety attitudes. All data analyses were processed through SPSS AU.

3 Results

3.1 Common method bias test

The results indicated that the first unrotated factor accounted for 29.720% of the total variance, which was less than 40% of the total variance explained (41). Accordingly, this study did not demonstrate a significant common method bias.

3.2 Descriptive statistics and correlation analysis of variables

The results of the correlation analysis are presented in Table 2. A significant negative correlation was observed between safety attitude

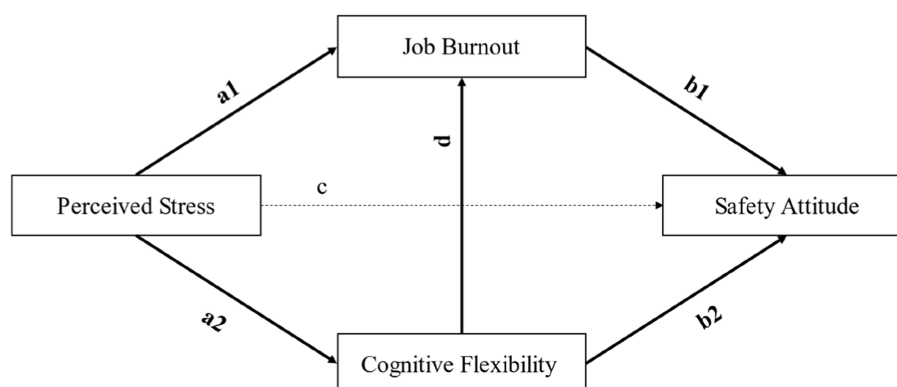


FIGURE 1
Path analysis of the hypothesis model.

TABLE 2 Descriptive statistics and correlation coefficients.

Variables	Mean	S. D.	1	2	3	3.1	3.2	3.3	4
Safety Attitude (1)	3.732	0.606	1						
Perceived Stress (2)	2.754	0.681	−0.330**	1					
Job Burnout (3)	3.068	0.965	−0.535**	0.672**	1				
JB-Emotional Exhaustion (3.1)	3.457	1.401	−0.432**	0.520**	0.849**	1			
JB-Depersonalization (3.2)	3.049	1.244	−0.461**	0.587**	0.873**	0.699**	1		
JB-Reduced Personal Accomplishment (3.3)	2.759	0.995	−0.396**	0.516**	0.680**	0.293**	0.396**	1	
Cognitive Flexibility (4)	3.588	0.413	0.503**	−0.553**	−0.542**	−0.363**	−0.448**	−0.508**	1

* $p < 0.05$, ** $p < 0.01$. The darker the color, the stronger the correlation. The lighter the color, the weaker the correlation.

and perceived stress (−0.330**). Similarly, job burnout was found to correlate positively with perceived stress (0.672**), while it also displayed a significant negative correlation with safety attitude (−0.535**). Cognitive flexibility was significantly negatively correlated with perceived stress (−0.553**) and positively correlated with safety attitude (0.503**). Additionally, a significant negative correlation was noted between cognitive flexibility and job burnout (−0.542**). All correlations specified in the hypotheses were confirmed.

3.3 Stepwise regression model for safety attitude

Using safety attitude as the dependent variable and perceived stress, job burnout, and cognitive flexibility as independent variables, regression analysis was conducted. The model was found to be statistically significant ($F(2,103) = 27.824, p < 0.001$). The statistical results revealed that perceived stress did not have a significant impact on safety attitude. However, job burnout ($\beta = -0.372, p < 0.001$) and cognitive flexibility ($\beta = 0.302, p = 0.002$) were observed to significantly influence safety attitude. These findings are consistent with the study's hypotheses, suggesting that perceived stress influences safety attitude through the mediating effects of job burnout and cognitive flexibility.

3.4 Path analysis results

Linear regression reflects the direct relationship between independent and dependent variables. However, the relationships between variables are often intricate. It is challenging to express all these relationships with a single regression model. Path analysis is then considered.

Drawing on the literature review and the proposed hypotheses, the path model constructed in this study encompasses several routes: (1) perceived stress directly influences safety attitudes, (2) perceived stress affects safety attitudes indirectly through job burnout, (3) perceived stress impacts safety attitudes indirectly via cognitive flexibility, and (4) perceived stress affects job burnout through the mediating effect of cognitive flexibility, which in turn influences safety attitudes.

The results of the path analysis, as depicted in Figure 2, aligned with those from the stepwise regression analysis. The path from perceived stress to safety attitude was not significant, whereas all other paths were significant. These findings are in perfect agreement with the hypotheses, suggesting that perceived stress influences safety attitude through the mediating effects of cognitive flexibility and job burnout.

To further validate the reliability of this hypothesized model, the path from cognitive flexibility to job burnout was removed experimentally. As shown in Figure 3, all path coefficients remained significant, and their magnitudes were not notably different, affirming the robustness of the model. Additionally, the removal of this path led to a decrease in the model's R^2 , reinforcing the notion that the chain-mediation model more accurately represents the mechanism through which perceived stress affects safety attitude.

To delve deeper into the roles played by the three dimensions of job burnout and cognitive flexibility in mediating the relationship between perceived stress and safety attitude, a comprehensive path analysis was performed on the individual dimensions of job burnout. The model's Goodness-of-Fit Index (GFI) was 0.902, indicating a good fit for the model.

As illustrated in Figure 4, significant associations were found between perceived stress and the three dimensions of job burnout. Notably, emotional exhaustion and depersonalization were identified as the dimensions that significantly impact safety attitudes. Furthermore, the influence of cognitive flexibility on job burnout was predominantly mediated by the dimension of Reduced Personal Accomplishment.

4 Discussions

4.1 Negative relationship between perceived stress and safety attitude

A negative correlation between pilots' perceived stress and safety attitude was identified in this study, which is consistent with findings from previous research (10, 11). In other words, as higher levels of stress are experienced by pilots, their safety attitudes tend to deteriorate. Similar to relationships between stress and attitude uncovered in other studies (42–44), the link between stress and safety

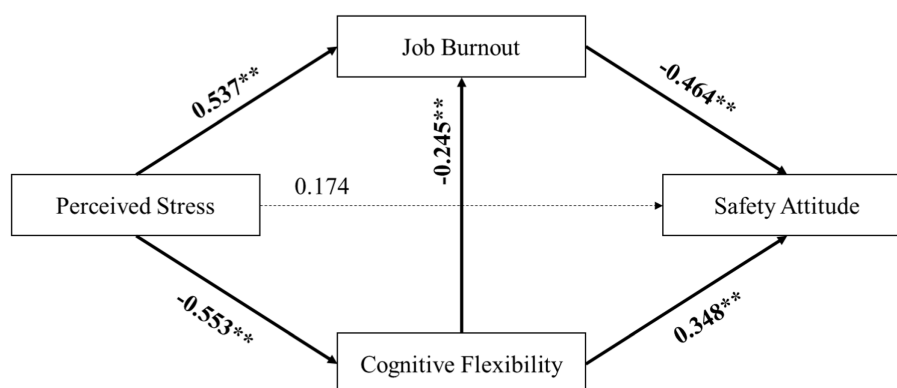


FIGURE 2
Path coefficient of the hypothesis model.

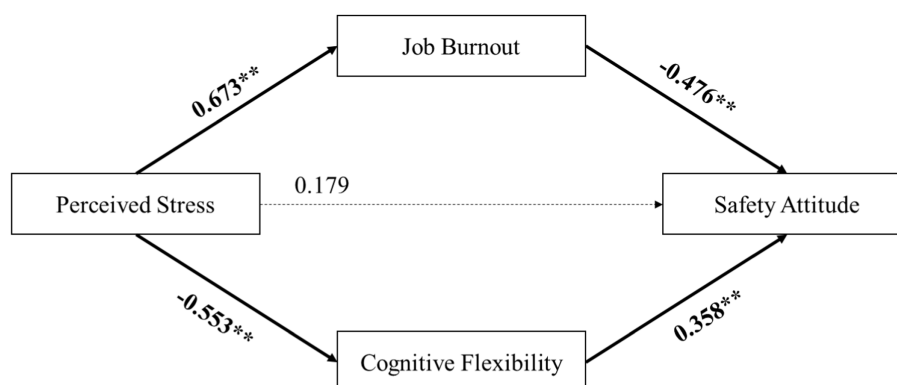


FIGURE 3
Path coefficient of the alternative model.

attitude is influenced by multiple variables. Further analysis of the relationship between pilots' perceived stress and safety attitude revealed that the impact is not directly correlated; the negative effects of perceived stress may need to go through intermediate processes before influencing safety attitude. This finding emphasizes the importance of in-depth research into the mechanisms between pilots' perceived stress and safety attitudes. Gaining an understanding of these mechanisms is crucial so that more effective recommendations for pilot stress management can be provided. Doing so enables the targeted development of training programs that enhance a pilot's ability to cope with high-pressure environments, thereby fostering the formation of positive safety attitudes, effectively reducing accident risks, and elevating aviation safety standards. Therefore, a thorough investigation into the relationship between pilot stress and safety attitudes holds significant theoretical and practical value for stress management and accident prevention.

4.2 Mediating effect of job burnout

Compared to other occupations, pilots work in a distinctive physical environment, subjecting them to increased physical exhaustion and the need to manage multiple tasks efficiently, along

with various stressors related to passenger safety (27). Additionally, pilots face an overwhelming workload, which includes demanding flight training and unpredictable work schedules, among other challenges. As a group susceptible to work-related exhaustion, pilots are prone to depleting their resources excessively when faced with high job demands, heightening their susceptibility to job burnout (45–47). Previous research has shown that employees with high levels of burnout are more likely to be troubled by negative emotions and attitudes, and they tend to approach organizational safety recommendations with skepticism and a negative attitude (48, 49). Consistent with the research hypothesis, when pilots are in a state of job burnout, safety attitude, considered beyond the operational tasks of flying, diminishes in interest and enthusiasm. Content of safety attitude may be perceived as unnecessary outside their job scope, pessimistic expectations about behavioral outcomes are held, and a resource-conservative strategy to reduce their level of engagement in work-related safety behaviors tended to be adopted (16, 50), adopting an attitude of neglect or avoidance toward safety-related activities.

The detailed analysis of the three dimensions of job burnout in this study supports this explanation. Significant correlations were found between perceived stress and emotional exhaustion, depersonalization, and reduced personal accomplishment in terms of burnout. However, concerning the mediating impact on safety

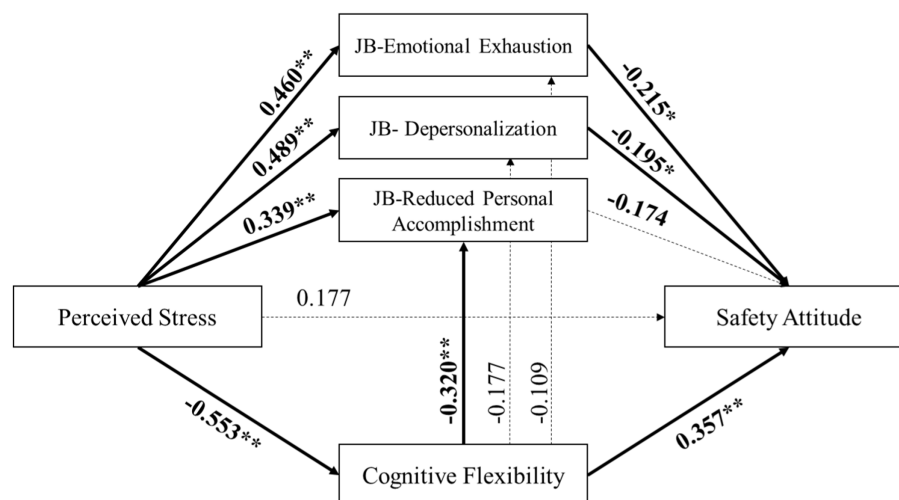


FIGURE 4
Path coefficient of the detailed model.

attitude, it is primarily emotional exhaustion and depersonalization that come into play, revealing that different dimensions of job burnout have varying effects on attitude formation (51, 52). In situations of job burnout, individuals tend to avoid additional tasks due to emotional exhaustion and a low sense of responsibility toward work (53), resulting in poorer safety attitudes. Combined with social exchange theory (54), when individuals perceive that the expected rewards are not provided by the organization, they may reduce work engagement and safety behaviors as a form of “punishment” for the organization. Therefore, to prevent pilot burnout, intervention should focus on emotional exhaustion and depersonalization, enhancing organizational support and fostering positive social exchange relationships.

4.3 Mediating effect of cognitive flexibility

Consistent with the hypothesis, pilots experiencing stress may encounter a decline in cognitive flexibility, impacting their cognitive processes related to flight tasks and safety concerns. Conversely, reducing perceived stress may result in improved cognitive flexibility, thereby enhancing safety attitudes. This aligns with the findings of a study on cognitive flexibility training by Fornette et al. (55). Following the training, pilots exhibited improved cognitive flexibility, which positively influenced emotional regulation and significantly enhanced flight performance scores. These results highlight the behavioral and attitudinal benefits associated with increased cognitive flexibility among pilots during uncertain flight situations (27). Considering the physiological mechanisms of cognitive flexibility (56, 57), it requires the involvement of the prefrontal cortex in regulation. Prolonged stress and negative emotions may lead to a decline in prefrontal cortex function. Consequently, pilots with low cognitive flexibility might adhere to their thinking patterns, strategies, and behaviors when facing flight pressure, making it challenging to cope with stress. This, in turn, leads to a deterioration of their psychological state, a reduction in confidence and responsibility for flight safety, and a decrease in

proactive and positive attitudes toward flight safety. On the other hand, pilots with high cognitive flexibility can adapt their thinking patterns, strategies, and behaviors flexibly when facing flight pressure (27), effectively alleviating stress, maintaining a positive psychological state, enhancing confidence and responsibility for flight safety, and increasing proactive and positive attitudes toward flight safety.

Cognitive flexibility can be enhanced through cognitive-behavioral interventions (29), as studies on prefrontal functioning and posttraumatic stress disorder demonstrate increased flexibility after treatment (27). Therefore, it is possible to mitigate the adverse effects of pressure on job burnout by enhancing pilots' cognitive flexibility.

4.4 Chain-mediation effect of flexibility and job burnout

The pathway from perceived stress through cognitive flexibility to job burnout, and finally to safety attitude, illustrates both the transmission and amplification effects of stress. This finding confirms Hypothesis H4, which posited that stress influences safety attitudes not only directly or indirectly but also through the chain mediation involving cognitive flexibility and job burnout. Specifically, perceived stress leads to a decrease in cognitive flexibility, rendering pilots more susceptible to job burnout, which in turn results in a deterioration of their safety attitudes.

Further analysis of the three dimensions of job burnout reveals that the influence of cognitive flexibility is predominantly evident in its impact on reduced personal accomplishment. Lower cognitive flexibility may hinder pilots' ability to effectively manage their workloads, necessitating increased effort to perform tasks and consequently leading to lower levels of personal accomplishment. This observation aligns with the proposed rationale for the association between cognitive flexibility and job burnout (38).

Based on these insights, it is evident that interventions aimed at enhancing the safety attitudes of pilots should focus on both improving cognitive flexibility and managing job burnout. Such

interventions are crucial to counteract the adverse effects of high stress levels on pilot safety attitudes.

4.5 Limitations

This study was conducted based on data from Chinese male pilots. In the future, the sample size can be expanded to include more countries to explore cross-cultural influences. Additionally, longitudinal research data and experimental data can be combined to further validate the paths mentioned in this study.

5 Conclusion

This study conducted a comprehensive exploration into the intricate mediating relationships among perceived stress, safety attitude, job burnout, and cognitive flexibility in commercial airline pilots. This research introduced, for the first time, insights into the roles of job burnout and cognitive flexibility, offering a profound understanding of the mechanisms underlying safety attitude formation among pilots.

The findings underscore the pivotal roles of job burnout and cognitive flexibility in mediating the relationship between perceived stress and safety attitude. It was specifically observed that perceived stress triggers emotional exhaustion and depersonalization, leading pilots to avoid tasks beyond their basic responsibilities. Furthermore, cognitive inflexibility contributes to a diminished sense of effectiveness in their work, culminating in feelings of low achievement. The combined influence of these factors significantly impacts pilots' safety attitudes.

This study provides airlines with a scientific theoretical path for better understanding and managing pilots' perceived stress and offers practical guidance for developing more effective pilot stress management strategies. In terms of enhancing pilots' psychological resources, airlines should focus on preventing and alleviating job burnout by enhancing organizational support, improving working conditions, and providing positive work feedback. This approach effectively addresses issues related to emotional exhaustion and apathy toward work. Additionally, the study recommends that airlines strengthen cognitive training activities to enhance pilots' cognitive abilities, enabling them to adapt to stress more flexibly, handle various work scenarios effectively, and thereby improve the proactivity and initiative of their safety attitudes.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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Ethics statement

The studies involving humans were approved by ethics committee of school of aeronautics. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ZY: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. ZK: Project administration, Supervision, Validation, Writing – review & editing. CH: Investigation, Software, Visualization, Writing – original draft. LZ: Investigation, Validation, Writing – review & editing. LP: Conceptualization, Writing – review & editing, Resources, Data curation, Investigation, Validation. WL: Conceptualization, Project administration, Resources, Supervision, Writing – review & editing.

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Conflict of interest

LP was employed by Zhuhai Xiangyi Aviation Technology Co., Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Short-term changes in chest CT images among individuals at low altitude after entering high-altitude environments

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Objective: To investigate the short-term changes in chest CT images of low-altitude populations after entering a high-altitude environment.

Methods: Chest CT images of 3,587 people from low-altitude areas were obtained within one month of entering a high-altitude environment. Abnormal CT features and clinical symptoms were analyzed.

Results: Besides acute high-altitude pulmonary edema, the incidence of soft tissue space pneumatosis was significantly higher than that in low-altitude areas. Pneumatosis was observed in the mediastinum, cervical muscle space, abdominal cavity, and spinal cord epidural space, especially the mediastinum.

Conclusion: In addition to acute high-altitude pulmonary edema, spontaneous mediastinal emphysema often occurs when individuals in low-altitude areas adapt to the high-altitude environment of cold, low-pressure, and hypoxia. When the gas escapes to the abdominal cavity, it is easy to be misdiagnosed as gastrointestinal perforation. It is also not uncommon for gas accumulation to escape into the epidural space of the spinal cord. The phenomenon of gas diffusion into distant tissue space and the mechanism of gas escape needs to be further studied.

KEYWORDS

plateau, plateau settlers, plateau environment acclimatization, spontaneous pneumomediastinum, spinal epidural space, multiple interstitial emphysema

Introduction

The decrease in oxygen partial pressure with increasing altitude is a well-known phenomenon. Individuals accustomed to living at low altitudes who suddenly find themselves at high-altitude experience a reduction in the diffused oxygen through their alveoli, leading to a decrease in oxygen saturation. As a result of this hypoxia, people commonly experience various physiological reactions, including headache, dizziness, nausea, vomiting, palpitations, and shortness of breath (1). When individuals present with chest discomfort, chest CT examination is the preferred imaging method as it can accurately depict structural abnormalities in the heart and lungs. While it is generally accepted that changes in the heart and lungs at high-altitude occur due to chronic high-altitude adaptation, only a few isolated cases have been reported during the early stages of this process (2, 3). Moreover, it is mostly related to aviation flight (4–7). Therefore,

we aim to conduct a comprehensive cross-sectional survey to investigate whether there are abnormal changes in CT images and to assess the extent of chest discomfort during the early phase of acclimatization to the plateau environment.

Materials and methods

Data collection was conducted at Ali District People's Hospital (located at an altitude of 3,670 meters) from January 2019 to May 2021. The retrospective study received approval from The Ethics Committee of The General Hospital of Western Theater Command Hospital. The written informed consent from the patients was waived. All the methods were carried out in accordance with relevant guidelines and regulations to ensure full patient and family understanding of the experimental procedures and their rights.

Inclusion criteria: (1) Migrant workers and tourists residing in low-altitude areas in central and eastern China must be over 18 years of age and have a living environment below 700 meters. (2) The first chest CT examination was performed within 1 month after arrival at the plateau. (3) With no history of cardiopulmonary disease and chest trauma.

Exclusion criteria: (1) Inadequate image quality for accurate diagnosis. (2) Patients who discontinued their participation during the study.

We also collected baseline data such as gender, age, and symptoms of patients.

Image acquisition and image diagnosis

All patients completed an outpatient medical history collection, inquiry, and physical examination. A chest CT scan was performed using a German Siemens SOMATOM Definition AS 64-slice CT scanner. The scanning range extended from the upper edge of T1 to the lower edge of the L1 spinous process. Parameters for the scan were as follows: (1) Tube voltage was usually set to 120 kV, but for patients with a thin body type, it could be set to 100 kV. For patients with an obese body type, it could be set between 120 and 140 kV. (2) Tube current was automatically regulated to ensure that CTDIvol was less than 4 mGy. (3) The display field (DFOV) was set to 33–35 cm. (4) The acquisition method used was volume acquisition with an acquisition layer thickness of 5 mm and an acquisition interval of 5 mm. Additionally, conventionally reconstructed 1–1.25 mm thin layer images were transmitted to PACS and workstations for backup. (5) The reconstruction algorithm used for the lung window was the lung algorithm with a convolution kernel B50, while the standard algorithm was used for the mediastinal window (soft tissue window).

To evaluate the presence or absence of pulmonary exudative lesions, pneumothorax, pleural effusion, cardiac morphology, mediastinum, and chest wall structure, two radiologists with more than 5 years of experience double-blindly read and scored the above indicators.

Result

The study was approved by the ethics committee of our hospital. We retrospectively analyzed the chest CT examination data of 3,587 subjects (3,007 males, age 19–56, average

age \pm SD = 35.40 ± 10.29) from January 2019 to May 2021 admitted to a medical station located in Ali, Tibet. This hospital is located at an elevation of about 3,670 meters, its service regions range from 3,000 to 5,400 meters, and the annual average temperature of Ali was -9°C . Out of a total of 3,587 cases, 94 individuals showed spontaneous pneumatosis (SP) in various tissue spaces, representing 2.62% (94 out of 3,587) of the total cases. The manifestations included subcutaneous emphysema (SE) in the neck, face, trunk, intra-vertebral canal, and pneumomediastinum (SPM).

The individuals with SP included in our study were 19–51 years old (average age = 29.36, SD = 7.41), and among them, 9 cases ≤ 20 -year-old, 40 cases were 21–30-year-old, 23 cases were 31–40-year-old, 16 cases were 41–50-year-old, and 6 cases > 50 -year-old. Seventy-seven of 94 cases were male (77/94, 81.91%). The duration of these individuals stayed at Ali was as follows: 22 cases < 2 weeks, 36 cases were 2–4 weeks, 25 cases were 4–8 weeks, and 11 cases were > 8 weeks. No obvious predisposing cause was found in 90 cases (90/94, 95.74%), and 1 case with fever (1/94, 1.06%), 3 cases with trauma (3/94, 3.19%). The clinical manifestations are shown in Table 1.

For each case, the SP was independently evaluated by 2 radiologists (work experiences of whom were 21 years and 17 years respectively). The volume of SP was graded according to the following criteria: (i) mild pneumatosis, the short diameter of maximum cross-section ≤ 2 mm or the number of independent pneumatosis ≤ 5 ; (ii) moderate pneumatosis, the short diameter of maximum cross-section > 2 mm and ≤ 5 mm or the number of independent pneumatosis > 5 and ≤ 10 ; (iii) severe pneumatosis, the short diameter of maximum cross-section > 5 mm or the number of independent pneumatosis > 10 . Possible disagreements were solved by consensus. The diagnosis results were as follows: 40 cases (40/94, 42.55%) were mild pneumatosis, 24 cases (24/94, 25.53%) were moderate pneumatosis and 30 cases (30/94, 31.91%) were severe pneumatosis. The locations of SP were also concluded (see Figure 1). In addition to SP, we also identified 3 cases with pneumon-edema (3/94, 3.19%), 3 cases with pulmonary bulla (3/94, 3.19%), 1 case with pneumonia (1/94, 1.06%), and 87 cases with negative CT signs in lungs (87/94, 92.55%). Moreover, subphrenic-free air was found in 14

TABLE 1 Main clinical manifestations in patients with spontaneous pneumatosis.

Clinical features	Frequency	Proportion (%)
Negative	21	22.3
Cough	16	17
Dyspnea	13	13.8
Chest pain	13	13.8
Oppression in chest	12	12.8
Pharyngodynia	9	9.6
Epigastric pain	5	5.3
Palpitation	3	3.2
Hyperpyrexia with chills	1	1.1
Vertigo	1	1.1

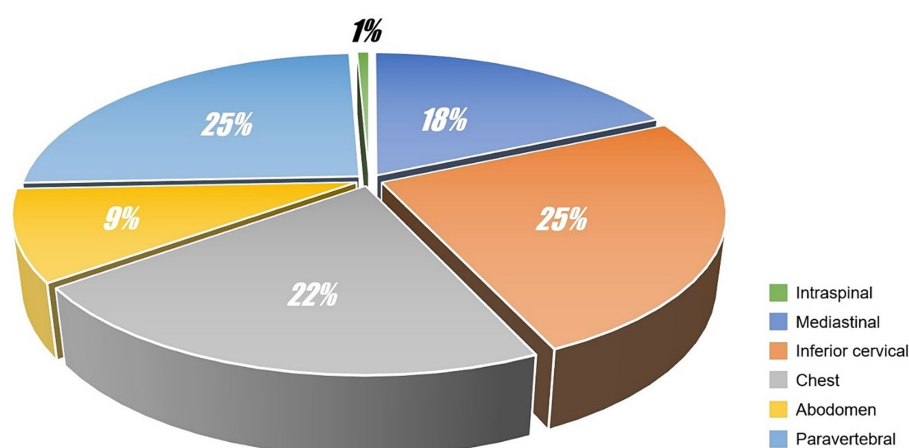


FIGURE 1
Location distribution of spontaneous pneumatosis.

cases (14/94, 14.89%), and 9 cases (9/14, 64.29%) were misdiagnosed as gastrointestinal perforation.

Discussion

Plateau and alpine areas above 3,000 meters in western China comprise approximately one-sixth of China's total land area. With the recent development of western China, there has been an increase in the construction of engineering projects and the growth of the tourism economy in these regions. Consequently, a significant number of people from lower altitudes are now traveling to the western high-altitude regions.

In addition to pulmonary edema, brain edema, and other common high-altitude-related diseases, the incidence of subcutaneous emphysema (SE) is also significantly higher in high-altitude areas compared to low-altitude areas. This may be attributed to the low temperature, low pressure, and hypoxic conditions prevalent in high-altitude environments. To the best of our knowledge, this is the first cross-sectional report presenting a large amount of data on SP affecting multiple tissue spaces at high-altitude.

Most SP cases involve young and middle-aged males, primarily engineers and tourists who have recently arrived in highland areas from lowland regions (with an adaptation time of less than 3 months), soldiers, and a few local residents. Due to the extreme natural environment and challenging conditions, the older adult, weak individuals, women, and children rarely venture into the plateau. Our data suggests that the incidence of SP affecting multiple tissue spaces during the altitude acclimatization period is significantly higher than that observed in a stable lowland environment.

We hypothesize that these subcutaneous emphysemas (SEs) in various locations may originate from spontaneous pneumomediastinum (SPM). SPM is a rare, self-limiting condition characterized by the presence of free air within the mediastinum without any association with chest trauma, surgery, or underlying diseases. Its incidence ranges from 0.002 to 0.125% (8).

The middle layer of the deep cervical fascia has thin and loose anatomical characteristics. The anterior tracheal fascia forms in

front of the trachea, the thyroid pseudocapsule forms in front of the thyroid gland, and the carotid artery is located on both sides. Various fascias, sheaths, and envelopes create gaps, providing the anatomical basis for the development of mediastinal and subcutaneous emphysema. The potential space within the mediastinum is interconnected, and the space surrounding the esophagus and trachea in the mediastinum extends into the potential space around the esophagus and trachea in the neck. It is also connected to the abdominal connective tissue and space through the thoracic rib triangle of the esophagus and lung. These anatomical features of the mediastinum make it susceptible to the development of mediastinal emphysema.

SPM is considered a result of alveolar rupture which generates free air that could flow into the mediastinum along the tunica-vaginalis around the pulmonary vasculature and could be triggered by breath-holding after inhalation and intense cough, and commonly seen in patients with bronchial asthma, bronchiolitis, or pertussis (9, 10). Most cases involved in our study had no clear clinical inducement. The atmospheric pressure at high-altitude is low, and intra- and extra-pulmonary pressure differences are imbalanced, which could result in pressures in some deep alveolar areas being greater than that in tissue space over a short term. Moreover, due to the decrease of oxygen levels at high-altitude, the atmospheric pressure and oxygen partial pressure above 3,000 meters are about 69.51 kPa (522.6 mmHg) and 14.55 kPa (109.4 mmHg) respectively, which are only about 68.76 and 68.81% of these pressures in sea level respectively, and in such environment, the ventilation of the body will be enhanced and the diffusion capacity of the alveolar membrane will be improved.

Extradural intra-vertebral pneumatosis was also observed in our study, as shown in Figure 2. To the best of our knowledge, this is the first study to report extradural intra-vertebral pneumatosis at high-altitude. Another noteworthy finding was the high proportion of SP cases accompanied by free intraperitoneal air, which is not commonly observed at low altitudes. This phenomenon is likely related to the management of dyspnea. Dyspnea is a common symptom experienced at high-altitude, and one of the conventional treatments for dyspnea is

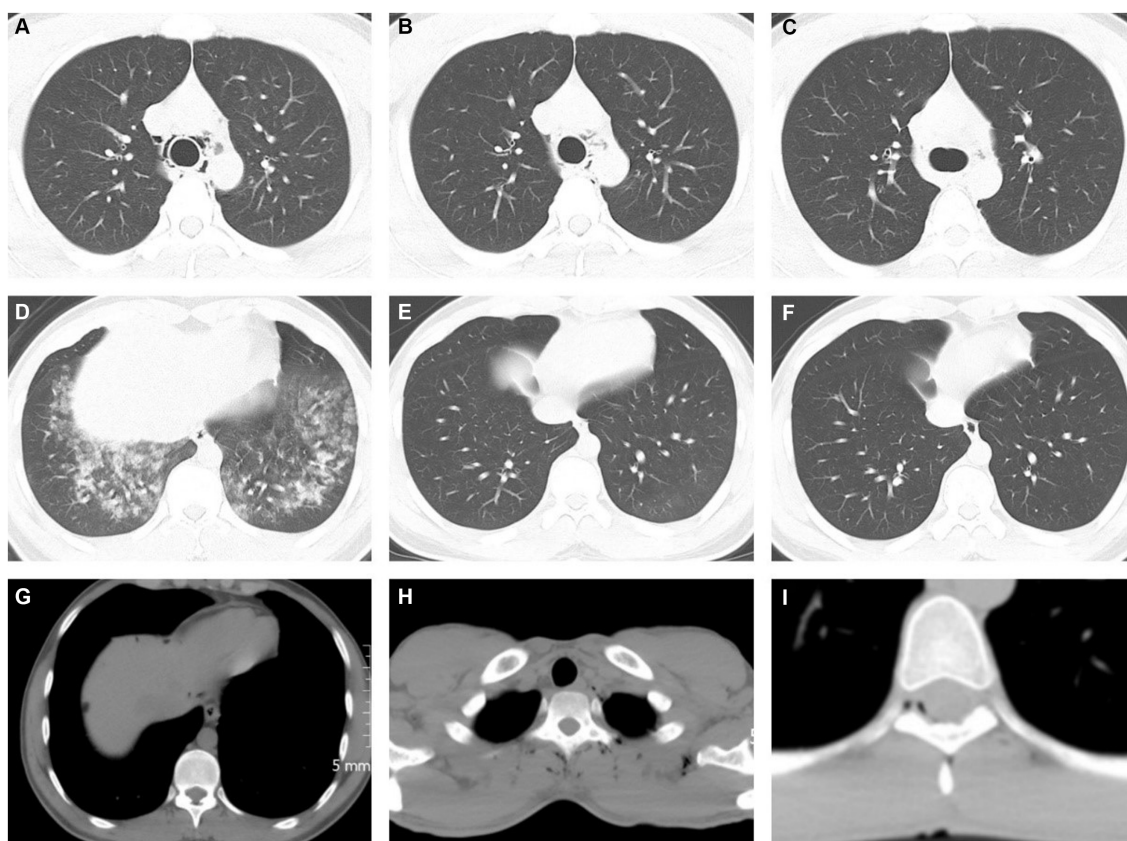


FIGURE 2

Chest CT images showed spontaneous pneumatosis. (A–F) 21years old, male, (A,D) showed a small volume of air in the mediastinum with pulmonary edema and large exudative lesions in both lower lungs, (B,E) on day 3, partial absorption of gas accumulation was reexamined, and pulmonary edema was significantly absorbed, (C,F) on day 7, pneumatosis and intrapulmonary exudate were reexamined for complete absorption. (G) A 25-year-old man presented with a patchy free gas shadow below the diaphragm at the edge of the liver. (H) A 23-year-old male with multiple gas accumulation near the spine and left periscapular space. (I) A 25-year-old man presents with pitted pneumatosis below the medial margin of the spinal canal.

lying down. The anatomical structure of the abdomen is relatively less compact, allowing for the diffusion of air in tissue spaces when in a supine position. This diffusion may not necessarily be directed toward the neck or shoulders, but can instead move downwards to the abdomen through the diaphragmatic hiatus. Due to a lack of understanding of SP in different tissue spaces in primary healthcare settings, misdiagnoses can occur. For example, in our study, 9 cases with subphrenic free air were initially misdiagnosed as gastrointestinal perforation, resulting in 5 patients receiving incorrect treatment for gastrointestinal perforation in the clinic. Additionally, we identified 3 cases of SPs in the paravertebral interosseous space (Figure 1), which did not resolve or decrease after 7 days. However, SPM alone cannot fully explain these observed signs. We speculate that factors related to the plateau environment and the composition of the gas within the pneumatosis may play critical roles in the occurrence of SP in these rare locations.

It is important to highlight that high-altitude can lead to the development of spontaneous pneumatosis (SP) in different tissue spaces, including pneumomediastinum, cervical pneumatosis, and thoracic pneumatosis, even in healthy individuals. The hypoxic and low-pressure environment of the plateau may represent an independent risk factor for the development of spontaneous mediastinal emphysema (11).

According to Boyle's law (12), which states that as cabin pressure decreases at higher altitudes, the volume of gas inside the lungs increases. This increase in volume can potentially lead to lung injury. However, in our patient, we were unable to definitively determine the exact cause of pneumomediastinum and pneumopericardium. We hypothesize that the patient, who may have had weakened or disrupted organ barriers, experienced air leaks as a result of the altitude change during early migration to the plateau. Another possible explanation could be that the air leak was caused by the rupture of an alveolar bleb due to changes in intra-thoracic pressures at higher altitudes.

After the onset of the plateau, several factors contribute to the occurrence of spontaneous pneumomediastinum (SPM). Firstly, the pulmonary circulation is the first to react to high-altitude exposure and undergoes changes in response to acute, continuous, and chronic stages of high-altitude hypoxia. This is a crucial aspect in the development of medical issues associated with acute and chronic high-altitude exposure, as it helps the body adapt to the low-pressure hypoxic environment of the plateau. The neuro-endocrine mechanism of the pulmonary circulation is one of the earliest to undergo changes (9). Secondly, upon entering the plateau, the airway resistance and total lung resistance decrease due to the low

pressure, deep and rapid breathing, and reduced turbulence. At an altitude of 3,400 m, the airway resistance can decrease by 17%. Furthermore, at an altitude of 5,000 m, there is a significant increase in maximum expiratory flow (PEF). According to the Macklin theory (13), certain inducing factors such as strenuous exercise or sudden changes in atmospheric pressure can lead to an increase in intra-alveolar pressure, causing alveolar rupture. This results in the release of air from the alveoli, which then peels off the vascular sheath and accumulates in the hilum, leading to the formation of mediastinal emphysema. If the gas pressure in the mediastinum becomes too high, the gas can diffuse along the neck, causing subcutaneous emphysema in the neck, face, and even the trunk (14, 15).

It should be acknowledged that the survey data is predominantly comprised of male migrant workers. The plateau's working environment is notably challenging, and migrant workers are primarily involved in infrastructure projects, resulting in minimal participation from female migrant workers in the survey. Although there are a few female tourists, their representation is minimal, leading to biased data. Therefore, the occurrence of HAPE and SPM may be linked to strenuous manual labor, and there is insufficient evidence to demonstrate gender differences. In future studies, we will allocate more time to conduct a thorough and detailed classification of gender and age.

Conclusion

By analyzing this group of cases, we have determined that CT examination is a reliable method for diagnosing early lung changes related to the plateau environment. It can also help identify complications. In addition to acute high-altitude pulmonary edema, spontaneous mediastinal emphysema (SPM) often occurs when individuals from low-altitude areas adapt to the high-altitude environment. Gas escaping to the abdominal cavity can be misdiagnosed as gastrointestinal perforation, and gas accumulation escaping into the epidural space of the spinal cord is not uncommon. The phenomenon of gas diffusion into distant tissue spaces and the mechanism of gas escape require further study. To improve the understanding and prevention of these diseases, we recommend the following preventive measures for people living in low-altitude areas (16–18): (1) People at high-altitude should avoid strenuous exercise and coughing forcefully. In cases of severe altitude sickness, appropriate oxygen therapy should be administered. (2) Stepwise adaptation is recommended. Individuals should undergo 1 week of training at an altitude of approximately 3,000 meters before ascending to higher altitudes. (3) Strengthening protection, eliminating fear, avoiding excessive mental stress, and ensuring adequate sleep are important. (4) Improving awareness of the disease is crucial. For example, chest pain should prompt immediate chest CT examination to rule out potential issues. X-ray examinations have a high rate of missed diagnosis. (5) In addition to treating the primary disease, timely mediastinal or subcutaneous drainage and decompression can relieve tension mediastinal emphysema. A comprehensive and overall treatment approach should be adopted. With early diagnosis and comprehensive treatment, a cure can be achieved. Our report provides valuable insights for the accurate diagnosis and management of spontaneous pneumomediastinum in various tissue spaces. As human

activities at high-altitude increase, further research in this field is necessary.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by The Ethics Committee of General Hospital of Western Theater Command. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because this is a retrospective observational study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

PW: Data curation, Formal analysis, Writing – original draft, Writing – review & editing. ZZ: Formal analysis, Funding acquisition, Writing – original draft. JWu: Data curation, Investigation, Methodology, Writing – original draft. JWa: Data curation, Investigation, Methodology, Supervision, Writing – original draft. RJ: Project administration, Writing – review & editing. FD: Conceptualization, Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing – review & editing.

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The ground reaction force pattern during walking under vestibular-demanding task with/without mastoid vibration: implication for future sensorimotor training in astronauts

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Background: The Sensory Organization Test condition 5 (SOT5) assesses an astronaut's vestibular function pre-/post-spaceflight but has a ceiling effect and mainly evaluates standing balance, neglecting the challenges of walking during space missions. A Locomotor Sensory Organization Test (LSOT) has been developed, mirroring the SOT concept but tailored to assess vestibular function during walking. This study aims to advance current knowledge by examining changes in ground reaction force (GRF) during normal walking (LSOT1) and walking in LSOT5 (vision blocked and treadmill speed varied), both with and without mastoid vibrations.

Methods: Sixty healthy adults were recruited and divided into two groups: one with mastoid vibration and one without. GRF peaks and respective variabilities were analyzed in the vertical (V), anterior-posterior (AP), and medial-lateral (ML) directions during stance cycles. The effects of LSOTs and mastoid vibration on each dependent variable were assessed using Friedman's two-way analysis of variance by ranks.

Abbreviations: SOT, Sensory organization test; LSOT, locomotor sensory organization test; V1, the mean of the first peaks of GRF in the vertical direction; V2, the mean of the second peaks of GRF in the vertical direction; AP1, the mean of the first peaks of GRF in the anterior-posterior direction; AP2, the mean of the second peaks of GRF in the anterior-posterior direction; ML1, the mean of the first peaks of GRF in the medial-lateral direction; ML2, the mean of the second peaks of GRF in the medial-lateral direction; V1V, the variability of the first peaks of GRF in the vertical direction; V2V, the variability of the second peaks of GRF in the vertical direction; AP1V, the variability of the first peaks of GRF in the anterior-posterior direction; AP2V, the variability of the second peaks of GRF in the anterior-posterior direction; ML1V, the variability of the first peaks of GRF in the medial-lateral direction; ML2V, the variability of the second peaks of GRF in the medial-lateral direction.

Results: The findings revealed that: 1) Walking in LSOT5 increased the variabilities of GRFs regardless of the administration of mastoid vibration; 2) the application of mastoid vibration reduced the amplitude of GRF peaks; and 3) walking in LSOT5 while receiving mastoid vibration was the most challenging task compared to all other tasks in this study.

Conclusion: The results indicated that analyzing GRF can detect changes in the strategy of balance control across different sensory-conflicted conditions. The findings could be beneficial for assessing the vestibular function pre- and post-space missions and planning for future sensorimotor training programs aimed at enhancing astronauts' abilities to navigate unpredictable sensory-conflicted conditions.

KEYWORDS

locomotor sensory organization test, gait stability, treadmill-induced perturbations, ground reaction force, vestibular function

1 Introduction

In 1969, Astronaut Neil Armstrong initiated his descent down the ladder and articulated, “That is one small step for a man, but one giant leap for mankind.” Subsequently, another astronaut, Dr. Edwin Aldrin, captured his own footprint on the lunar surface (https://nssdc.gsfc.nasa.gov/imgcat/html/object_page/a11_h_40_5878.html, assessed on 20 April 2024). While the footprint registers a depth of approximately one inch, it does not yield insights into the magnitude of the force exerted by Dr. Aldrin during routine ambulation under lunar gravity. On Earth, humans exhibit an extraordinary capacity to perceive gravity, orient themselves within their surroundings, and undertake sensory-motor activities, including walking and maintaining balance amidst challenging environmental conditions, such as darkness, diverse weather phenomena, or surfaces with varying textures such as sand, snow, or wet terrain. The vestibular system serves a pivotal role in detecting head movements, accelerations, and alterations in self-motion relative to gravitational forces (Messina et al., 2021). Additionally, the vestibulo-ocular reflex ensures ocular stability during head movements, thereby maintaining a steady retinal image of the surrounding environment regardless of head motion (Martines et al., 2021). Thus, in a subsequent lunar mission, Dr. Harrison Schmitt, a proficient astronaut, encountered challenges while traversing the lunar terrain, necessitating awkward maneuvers to regain stability (<https://www.youtube.com/watch?v=qZBdYp1O2DM>, assessed on 20 April 2024). There are a couple of possible reasons that may explain the gait instability experienced by astronauts during moonwalks: 1) changes in gravitational forces and 2) alterations in the center of mass location resulting from the spacesuit. For the rationale #1, the gravitational changes on the vestibular system reduce accuracy in detecting self-orientation (Carriot et al., 2021) and generate the inappropriate tilt of body orientation due to the changes in gravity (Reschke et al., 2017), potentially causing falls (e.g., Dr. Schmitt's example). Moreover, Tays et al. (2021) investigated the vestibular-related balance control in 15 astronauts who had spent approximately 6 months in space upon their return to Earth. Observations indicate that vestibular function takes at least 30 days to fully recover after an extended period of exposure to microgravity, unlike the other two sensory

systems (vision and somatosensory systems) (Tays et al., 2021). This highlights the challenge that vestibular function poses when traveling across different planets. However, none of these previous studies have addressed the impact of the spacesuit on gait or stance stability.

The Sensory Organization Test (SOT) has emerged as a pivotal component of clinical assessment for evaluating vestibular function in patients with various vestibular disorders, as extensively documented in prior research (Black et al., 1989; Goebel and Paige, 1989; Hytonen et al., 1989; Mulavara et al., 2013). This test encompasses one baseline and five sensory-conflicted conditions, including scenarios such as 1) eyes open on a fixed surface, 2) eyes closed on a fixed surface, 3) sway-reference vision on a fixed surface, 4) eyes open with sway-reference support, 5) eyes closed with a sway-reference surface, and 6) sway-reference vision with the sway-reference surface. The somatosensory function is discerned by comparing body sway between SOT1 and SOT2, while the visual function is evaluated by comparing sway between SOT1 and SOT4. Moreover, vestibular function has garnered particular interest in numerous studies examining astronauts pre- and post-space missions (Hupfeld et al., 2022; Tays et al., 2021; Shishkin et al., 2023). This evaluation often involves comparing sway between SOT1 and SOT5, employing the principle of simultaneously perturbing the visual and somatosensory systems to indirectly assess vestibular function (Horak, 2007). Horak (2007), in the textbook (Vestibular rehabilitation, third edition, chapter 3. Role of vestibular system in postural control in page 37) describes the SOT5 as: “Vestibular information gives a more accurate estimate of body position and motion under these circumstances (SOT5), and central nervous system (CNS) should rely more heavily on vestibular information for orientation.” Therefore, in following studies, this SOT5 has specifically been used to diagnose the patients with vestibular disorders (Nashner et al., 1982; Black and Nashner, 1984; Black et al., 1988; Shumway-Cook and Horak, 1986) because theoretically the Equilibrium Score should be lower in patients than in healthy controls. Despite its inception approximately 30 years ago, the practice of measuring disparities in sway between SOT1 and SOT5 remains a contemporary method for evaluating vestibular function in astronauts immediately post-spaceflight, as well as for assessing the restoration of balance control in astronauts after extended

spaceflight durations (approximately 6 months, Tays et al., 2021; Shishkin et al., 2023). Tays et al. (2021) indicate that microgravity environment resulted in a significant decrease in Equilibrium score in SOT5, indicating a malfunction of the vestibular system after staying microgravity in a period of time. However, a couple of concerns arise regarding this equilibrium score measure: the potential ceiling effect and its sensitivity (Grove et al., 2021). The limit of stability is approximately seven degrees posteriorly and five degrees anteriorly (approximately twelve degrees in range). Participants stepping off from the platform receive an equilibrium score of 0, indicating failure. Within this range, patients with vestibular deficits easily stepped off the platform, leading to only about 50% sensitivity to identify the vestibular deficits using SOT (Di Fabio, 1995). Indeed, these clinical observations of assessing vestibular function through SOT may not be directly applicable to evaluating changes in vestibular function induced by microgravity alterations. It remains reasonable to speculate that the time required for complete adaptation in vestibular function post-space mission could potentially be misinterpreted using SOT, despite its longstanding use in identifying vestibular function in astronauts pre- and post-space missions over the past couple of decades. Most of the aforementioned studies primarily focus on assessing vestibular function pre- and post-space missions while standing but not during walking. Therefore, it is still unknown when these astronauts fully recover their vestibular-related balance during walking. Also, if a walking task is involved in investigating the vestibular function after these astronauts complete their space missions, it typically consists of simple tasks with minimal vestibular demand, such as sit-to-stand, normal walking straight tasks, and obstacle negotiation tasks (Hupfeld et al., 2022). Therefore, it remains uncertain how the disrupted vestibular system (due to exposure to microgravity) affects balance control in astronauts mentioned above when walking under vestibular-demanding tasks, such as navigating dark and unstable surfaces, akin to walking on snowy and slippery ground in the dark of night on Earth.

Expanding upon the foundational principles of the SOT, Chien et al. (2014) devised the Locomotor Sensory Organization Test (LSOT) to assess dynamic balance control (sway) across various sensory challenging conditions. Similar to SOT, LSOT consists of six conditions:

1. Walking normally with full vision on a fixed-speed treadmill.
2. Walking with a blocked vision on a fixed-speed treadmill.
3. Walking with vision-perturbed surroundings on a fixed-speed treadmill.
4. Walking with full vision on a speed-varied treadmill.
5. Walking with blocked vision on a speed-varied treadmill.
6. Walking with vision-perturbed surroundings on a speed-varied treadmill.

For LSOT 5, participants walked on the treadmill with perturbations while wearing blackout goggles covered with a layer of 5% car-tinting vinyl, effectively blocking peripheral vision. A small amount of light was permitted to penetrate the goggles to simulate reduced lighting conditions, with light intensity reduced from approximately 150 lx (typical office lighting) to approximately 0.7 lx (comparable to the full Moon on a dark street without streetlights). Wearing this specific goggle reduces the visibility and further forces thirty healthy young individuals to increase the level

of active control by increasing the range of heel placements on treadmill between steps (Ren et al., 2022). This result indicates that the increase in active control of heel placement is attributed to a compensatory strategy that utilizes proprioceptive, somatosensory, and vestibular inputs to maintain dynamic balance in conditions of restricted vision. Furthermore, walking or standing in such limited visual environments has been shown to improve balance in patients with Parkinson's Disease (Tramontano et al., 2016; Bonni et al., 2019) and in individuals with unilateral lower-limb amputations (Vrieling et al., 2008).

However, it could be argued that the design of LSOT4-6 may have a potential drawback, as the changes in balance control during gait could be solely attributed to alterations in sudden acceleration by the treadmill rather than sensory conflicts. To address this, in the LSOT5 condition, the mean speed within treadmill-induced perturbations is set to 99.2% of the preferred walking speed, closely mirroring the preferred walking speed observed in LSOT1 (Wang et al., 2024). This method allows for the averaging out of any changes solely induced by sudden accelerations in LSOT5 compared to LSOT1. Wang et al. (2024) further observe that there is no significant difference in step length, which is highly related to treadmill speed because the differences in step length were averaged out. However, the margin of stability is significantly smaller in LSOT5 than LSOT1, indicating that walking in LSOT5 indeed triggers the sensory reweighting process (Wang et al., 2024). However, it can also be debated whether the vestibular system specifically plays a role in controlling balance in LSOT5. This argument can be explored by implementing vestibular stimulation through bilateral mastoid vibration (Lin et al., 2021; Sun et al., 2023). If walking in LSOT5 specifically involves balance control by the vestibular system, mastoid vibration would alter the balance control compared to conditions without mastoid vibration during walking. Based on Chien et al.'s findings, walking in LSOT5 with mastoid vibrations (MV), whether unilaterally or bilaterally applied, markedly increases the variability of the net center of pressure sway in both young adults (Chien et al., 2016) and older adults (Chien et al., 2017) compared to walking in LSOT5 without mastoid vibration. In fact, it has been proposed that any alterations in body acceleration prompt a reliance on the vestibular system (Wibble et al., 2020). Therefore, it can be explained that when walking in LSOT5, the Central Nervous System (CNS) may prioritize the vestibular system over the other two sensory systems to maintain balance.

In order to measure balance control during walking, ground reaction force (GRF) is commonly measured in patients with strokes (Chen et al., 2007; Hsiao et al., 2016; Kim and Eng, 2003), Parkinson's disease (Alam et al., 2017), peripheral arterial disease (Scott-Pandorf et al., 2007), and in those with disturbed unilateral vestibular systems (Magnani et al., 2021). As a result of stepping on the force plates while walking, the ground generated an equal and opposite reaction force for each foot, allowing the identification of the force applied to the ground and acceleration-related data to be obtained. During the initial single support phase, the center of mass was transferred from the lowest to its highest location, leading to a peak in the vertical direction (V1). Also, the second peak (V2) occurred during the late single support phase to slow and control the downward movement of the center of mass. It should be noted that the first peak in the anterior-posterior direction (AP1) represented

deceleration due to posterior shear force whereas the second peak demonstrated pushing off, which propelled the body forward. Also, when the heel strikes initially, there is a lateral thrust in the medial-lateral direction (ML). In the final push-off stage, a small lateral force was observed after the body moved over the stance limb. Specifically, Magnani et al. (2021) suggested that the vestibular system was critical to the control of GRFs in the ML direction while unilateral vestibular function was disrupted. Interestingly, the alterations in GRFs during walking under vestibular-demanding tasks, where both vestibular systems are perturbed bilaterally simultaneously, remain undiscovered. Understanding this knowledge gap could establish fundamental concepts of ground reaction force (GRF) applied under such conditions, thereby informing future space missions, such as walking on dark and quicksand surfaces on Mars. Since spatial-temporal gait parameters (Chien et al., 2014), the net center of pressure (Chien et al., 2016; Chien et al., 2017), heel placement (Hu and Chien, 2021), and margin of stability (Wang et al., 2024) have been investigated in LSOT1 and LSOT5, this study aimed to expand upon the existing knowledge by examining the changes in GRF while walking in LSOT5 (vestibular-demanding task) with and without MV (vestibular disruption).

A large, well-equipped facility such as NASA has the capability to measure changes in vestibular-related balance control in response to alterations in gravity. However, the costs associated with such measurements in vestibular-related balance control may not be justified in a typical biomechanical laboratory. Nonetheless, a viable and cost-effective method exists for assessing vestibular-related balance control in vestibular-perturbed and vestibular-demanding environments through the utilization of vestibular stimulation (mastoid process). Specifically, the application of mastoid stimulation has been demonstrated to increase the Center of Gravity (CoG) sway area in both young and older adults during standing (Lin et al., 2022; Zhang et al., 2024), as well as the variability of the net Center of Pressure sway area in both young and older adults (Chien et al., 2016; Chien et al., 2017). These findings affirm the feasibility of employing mastoid vibrations to disrupt vestibular function. Consequently, this study aimed to utilize bilateral MV to simulate scenarios wherein astronauts (serving as healthy controls in the present study) walk with an unreliable vestibular system due to fluctuations in gravity levels during vestibular-demanding tasks.

This study was supported by NASA as a pilot investigation focused on identifying force shifts during walking, particularly in relation to the vestibular system under sensory-conflicted conditions, to inform future research. To the best of our knowledge, this study is the first to examine how GRF patterns change when walking in a vestibular demanding environment, both with and without vestibular disruption. Given the uncertainties involved, this study aimed to explore GRF patterns and their respective variability across all three directions. Hence, the aims of this study were to determine 1) whether walking in vestibular-demanding environment (LSOT5) altered the GRF patterns compared to walking normally (LSOT1); 2) when the vestibular system was disrupted bilaterally, what changes in GRF patterns would be observed in normal walking (LSOT1) and in vestibular-demanding conditions? Enhanced comprehension of GRFs could assist physicians and astronauts in discerning

the role of vestibular function in controlling force shifts during walking in various gravity levels and vestibular-demanding environments. This study hypothesized that 1) walking in LSOT5 decreased the GRFs and increased the GRF variabilities; 2) applying MV decreased the GRFs and increased the GRF variabilities; and 3) LSOT5 with bilateral MV would be the most challenging task compared to other conditions, indicating that LSOT5 can be used to identify the deteriorations in vestibular system.

2 Materials and methods

2.1 Participants

In this investigation, a cohort of sixty young adults participated. These individuals were divided into two distinct groups: 1) the no mastoid vibration group (NoMV) and 2) the mastoid vibration group (MV). The NoMV group comprised 15 males and 15 females, with an average participant age of 22.9 ± 2.11 years (range: 8), an average height of 1.70 ± 0.07 (range: 0.28) m, and an average weight of 66.59 ± 8.52 (range: 32) kg, exhibiting a preferred walking speed of 1.48 ± 0.22 (range: 0.8) m/s. Correspondingly, the MV group consisted of 16 males and 14 females, with comparable demographic characteristics: an average age of 24.3 ± 2.89 (range: 10) years, an average height of 1.71 ± 0.08 (range: 0.31) m, an average weight of 67.87 ± 7.5 (range: 30) kg, and a preferred walking speed of 1.52 ± 0.27 (range: 1.1) m/s. It has been shown that the walking speed may affect the perception of vestibular function (Anson et al., 2019). Therefore, this study attempted to match the age, height, weight and preferred walking speeds between groups as close as possible to limit the effect of confounding factors (Table 1). Importantly, none of the participants reported any ankle, knee, or hip injuries that could potentially influence their gait patterns by self-reporting. Moreover, they had no history of falls in the preceding year and exhibited no deficits in visual, somatosensory, or vestibular functions by self-reporting. Participants were required to achieve a Dizziness Handicap Inventory score of 0, indicating the absence of vestibular impairments. Otherwise, the participant would have been excluded from the study. It should be noted that this score on the Dizziness Handicap Inventory was for inclusive criteria and this score was not the dependent variable in the present study. Ethical considerations were rigorously observed throughout the study, as evidenced by the approval of the University of Nebraska Medical Center Institutional Review Board (IRB# 340-10-FB). Prior to data collection, each participant voluntarily provided informed consent by signing a consent form on the day of the experiment.

For the purpose of estimating the sample size, two sources were used: 1) prior studies and 2) power estimation using G*Power (URL: <http://www.gpower.hhu.de/>). From the Chien et al.'s study (2016), which investigating the net center of pressure area variability calculated by force plate under different LSOT x MV conditions in twenty healthy young individuals, the partial eta squared values were 0.982 for the effect of LSOT effect, 0.913 for the effect of MV, and 0.388 for the interaction between the effect of LSOT and the effect of MV. These partial eta squared values indicated the large effect size (>0.138) according to the Cohen's textbook (1988). Also, from Lu

TABLE 1 Participants' information.

	Age (yrs)		Height (m)		Weight (kg)		Walking speed (m/s)	
	Group#1	Group#2	Group#1	Group#2	Group#1	Group#2	Group#1	Group#2
	24	30	1.68	1.66	57	51	1.2	1.2
	23	23	1.63	1.66	75	75	1.3	1.3
	22	20	1.82	1.83	75	70	1.5	1.5
	22	22	1.77	1.71	49	51	1.3	1.3
	27	28	1.67	1.69	45	75	1.5	1.5
	23	23	1.73	1.72	54	54	1	1.1
	25	25	1.76	1.78	74	71	1.8	1.9
	22	22	1.65	1.65	70	74	1.5	1.4
	24	23	1.78	1.79	73	75	1.7	1.7
	25	24	1.79	1.78	51	57	1.7	1.7
	26	30	1.56	1.59	76	75	1.6	1.6
	26	27	1.68	1.83	73	81	1.7	1.8
	21	28	1.68	1.71	77	74	1.7	1.7
	21	20	1.56	1.52	76	75	1.4	1.4
	20	26	1.74	1.8	67	66	1.3	1.3
	23	23	1.7	1.64	67	66	1.8	1.8
	20	20	1.72	1.7	68	67	1.5	1.5
	20	22	1.69	1.67	68	65	1.6	1.6
	22	23	1.68	1.68	63	66	1.1	0.8
	22	25	1.73	1.76	65	66	1.8	1.9
	22	23	1.76	1.8	70	72	1.3	1.4
	25	26	1.75	1.71	70	66	1.3	1.5
	22	25	1.72	1.72	57	61	1.7	1.8
	22	24	1.54	1.64	69	72	1.7	1.9
	25	27	1.76	1.82	66	66	1.3	1.2
	23	27	1.72	1.77	70	72	1.5	1.6
	22	22	1.61	1.66	76	75	1.7	1.9
	21	21	1.73	1.72	64	66	1.4	1.5
	21	21	1.71	1.7	64	61	1.3	1.4
	28	28	1.69	1.61	69	71	1.3	1.4
Avg	22.97	24.27	1.70	1.71	66.60	67.87	1.48	1.52
Std	2.11	2.90	0.07	0.08	8.52	7.51	0.22	0.27

TABLE 2 Means, Median, and Standard deviation of each dependent variables.

V1	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	1.25	1.28	1.17	1.17
Median	1.23	1.24	1.17	1.18
Standard Deviation	0.08	0.15	0.02	0.03
V1V	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	2.90	5.42	2.55	3.10
Median	2.47	4.73	2.38	2.86
Standard Deviation	1.02	3.45	0.83	0.91
V2	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	1.30	1.31	1.21	1.20
Median	1.28	1.28	1.22	1.20
Standard Deviation	0.09	0.15	0.04	0.04
V2V	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	2.07	4.33	2.23	5.37
Median	2.07	3.31	2.13	5.23
Standard Deviation	0.41	2.55	0.62	1.04
AP1	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	−0.31	−0.35	−0.29	−0.26
Median	−0.30	−0.34	−0.28	−0.27
Standard Deviation	0.07	0.07	0.05	0.04
AP1V	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	10.19	17.98	12.22	18.58
Median	9.27	17.04	12.35	17.38
Standard Deviation	3.00	4.50	3.66	4.46
AP2	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	0.32	0.34	0.28	0.28
Median	0.32	0.35	0.28	0.27
Standard Deviation	0.05	0.06	0.05	0.04

(Continued on the following page)

TABLE 2 (Continued) Means, Median, and Standard deviation of each dependent variables.

AP2V	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	8.21	15.32	10.89	17.03
Median	8.71	14.94	10.04	16.77
Standard Deviation	1.67	3.23	4.17	3.61
ML1	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	0.22	0.23	0.21	0.20
Median	0.22	0.23	0.22	0.21
Standard Deviation	0.05	0.04	0.03	0.03
ML1V	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	9.44	12.32	14.05	14.66
Median	9.11	11.98	13.66	13.57
Standard Deviation	2.49	3.77	4.69	3.95
ML2	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	0.23	0.25	0.23	0.21
Median	0.23	0.25	0.23	0.21
Standard Deviation	0.06	0.05	0.04	0.03
ML2V	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Mean	8.67	11.50	11.88	14.17
Median	8.94	11.13	12.03	13.31
Standard Deviation	1.84	3.06	3.81	3.86

et al., study (2022), which investigating the different MV effect on margin of stability (MOS) in twenty healthy young adults, the partial eta squared values were 0.755 for MOS in the anterior-posterior and 0.695 for MOS in the medial-lateral directions, indicating the large effect size. A power estimation using G*Power 3.1 was used to estimate the statistical power. The MANOVA for statistical test and *a priori*: compute required sample size–given alpha, power, and effect size for type of power analysis, and the effect size $f(v) = 0.565 \sim$ partial eta squared value = 0.059 were selected and the result showed that total sample size = 43 (22 for each group) could reach the power of 95%. Also, when 40 participants were recruited (20 per each group by aforementioned studies), the means (LSOT1: 0.32, LSOT5: 0.34, LSOT1MV: 0.29, LSOT5MV: 0.25) and standard deviations (LSOT1:

TABLE 3 Statistical Analysis, the bold fonts indicated the significance. The level of significance was 0.0007 for pairwise comparisons. S: significant. NS: not significant.

V1 (Friedman test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p = 0.039$ (NS)	$p < 0.0001$ (S)	$p < 0.0001$ (S)
LSOT5		X	$p < 0.0001$ (S)	$p < 0.0001$ (S)
Normal_ MV			X	$p = 0.943$
LSOT5_ MV				X
V1V (Friedman Test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p < 0.0001$ (S)	$p = 0.179$	$p = 0.152$
LSOT5		X	$p = 0.0011$ (NS)	$p < 0.0001$ (S)
Normal_ MV			X	$p < 0.0001$ (S)
LSOT5_ MV				X
V2 (Friedman Test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p = 0.845$	$p < 0.0001$ (S)	$p < 0.0001$ (S)
LSOT5		X	$p < 0.0001$ (S)	$p < 0.0001$ (S)
Normal_ MV			X	$p = 0.026$ (NS)
LSOT5_ MV				X
V2V (Friedman Test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p < 0.0001$ (S)	$p = 0.478$	$p < 0.0001$ (S)
LSOT5		X	$p < 0.0001$ (S)	$p = 0.0014$ (NS)
Normal_ MV			X	$p < 0.0001$ (S)
LSOT5_ MV				X

(Continued on the following page)

TABLE 3 (Continued) Statistical Analysis, the bold fonts indicated the significance. The level of significance was 0.0007 for pairwise comparisons. S: significant. NS: not significant.

AP1 (Mixed ANOVA, interaction: $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p = 0.0001$ (S)	$p = 0.073$	$p = 0.0006$ (S)
LSOT5		X	$p = 0.0002$ (S)	$p < 0.0001$ (S)
Normal_ MV			X	$p = 0.014$ (NS)
LSOT5_ MV				X
AP1V (Friedman Test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p = 0.0001$ (S)	$p = 0.023$ (NS)	$p < 0.0001$ (S)
LSOT5		X	$p < 0.0001$ (S)	$p = 0.605$
Normal_ MV			X	$p = 0.0001$ (S)
LSOT5_ MV				X
AP2 (Friedman Test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p = 0.041$ (NS)	$p = 0.006$ (NS)	$p = 0.007$ (NS)
LSOT5		X	$p < 0.0001$ (S)	$p = 0.0005$ (S)
Normal_ MV			X	$p = 0.673$
LSOT5_ MV				X
AP2V (Friedman Test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_ MV	LSOT5_ MV
Normal	X	$p < 0.0001$ (S)	$p = 0.006$ (NS)	$p < 0.0001$ (S)
LSOT5		X	$p < 0.0001$ (S)	$p = 0.069$ (NS)
Normal_ MV			X	$p < 0.0001$ (S)
LSOT5_ MV				X

(Continued on the following page)

TABLE 3 (Continued) Statistical Analysis, the bold fonts indicated the significance. The level of significance was 0.0007 for pairwise comparisons. S: significant. NS: not significant.

ML1 (Mixed ANOVA, interaction: $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Normal	X	$p = 0.039$ (NS)	$p = 0.781$	$p = 0.296$
LSOT5		X	$p = 0.054$	$p = 0.0064$ (NS)
Normal_MV			X	$p = 0.171$
LSOT5_MV				X
ML1V (Friedman Test, $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Normal	X	$p < 0.0001$ (S)	$p < 0.0001$ (S)	$p < 0.0001$ (S)
LSOT5		X	$p = 0.156$	$p = 0.019$ (NS)
Normal_MV			X	$p = 0.280$
LSOT5_MV				X
ML2 (Mixed ANOVA, interaction: $p < 0.001$)				
	LSOT1	LSOT5	LSOT1_MV	LSOT5_MV
Normal	X	$p = 0.042$ (NS)	$p = 0.669$	$p = 0.101$
LSOT5		X	$p = 0.075$	$p = 0.0018$ (NS)
Normal_MV			X	$p = 0.005$ (NS)
LSOT5_MV				X
ML2V (Friedman Test, $p < 0.001$)				
	Normal	LSOT5	Normal_MV	LSOT5_MV
Normal	X	$p < 0.0001$ (S)	$p = 0.0006$ (S)	$p < 0.0001$ (S)
LSOT5		X	$p = 0.690$	$p = 0.006$ (NS)
Normal_MV			X	$p = 0.027$
LSOT5_MV				X

Bold represents $p < 0.0007$.

0.06, LSOT5: 0.05, LSOT1MV: 0.05, LSOT5MV: 0.05) of first peak of GRF in the anterior-posterior direction were used to calculate the power using G*Power ($f(v) = 0.425$) and the result indicated that recruiting a total sample size of 60 participants (30 per each group) can reach 90% of power for interpreting the outcomes. Thus, in the current study, recruiting 30 participants in each group should have sufficient power to interpret the results in the current study.

2.2 Experimental setup

In this study, a treadmill equipped with two force plates (FIT5, Bertec Corp., Columbus, OH, USA) beneath two belts, one for each leg, was utilized to measure ground reaction force (GRF) during walking in the anterior-posterior (AP), medial-lateral (ML), and vertical (V) directions. Each leg had its independent force plate, and the sampling rate for ground reaction forces was 300 Hz. The Locomotor Sensory Organization Test (LSOT) comprised six conditions, as previously described in Chien et al.'s research on locomotor sensory organization test (Chien et al., 2014; Chien et al., 2016; Chien et al., 2017). In LSOT 5, the treadmill speed changed every 5–10 s to ensure at least five strides between each alteration in speed. This design was based on prior studies, which suggested that allowing at least four to five strides (around 5 s) between treadmill perturbations could mitigate the risk of falling and facilitate recovery from the perturbations (Forner Cordero et al., 2003). A maximum of 10 s (approximately 8–10 strides) between speed changes was implemented to create a continuous alteration in walking speeds for participants. Treadmill-induced perturbations were designed as follows (refer to Figure 1.): Step #1) time blocks were generated continuously and randomly until the sum of these values reached 120 s; Step #2) preferred walking speed (PWS) blocks were generated within a range of −20%–20% (positive values indicating acceleration, negative values indicating deceleration). This value was assigned to the time blocks and added to the previously generated values. The range of walking speed (80%–120% of PWS) was selected to avoid significant changes in gait patterns. In this study, 17-time interval blocks were established, and the speed alterations are depicted in Figure 1 (Chien et al., 2014; Chien et al., 2016; Chien et al., 2017; Hu and Chien, 2021; Wang et al., 2024). The sudden acceleration of the treadmill belt was set at 8 m/s^2 to induce the perturbations (Song et al., 2021), and these speed alterations were controlled by a customized visual basic script (Microsoft, Redmond, USA). Only LSOT one and five were utilized in this study to align with its objectives, focusing solely on investigating the vestibular system. For LSOT 5, participants walked on the treadmill with perturbations while wearing blackout goggles covered with 5% car-tinting vinyl, effectively blocking peripheral vision. A small amount of light was permitted to penetrate the goggles to simulate reduced lighting conditions, with light intensity reduced from approximately 150 lx (typical office lighting) to approximately 0.7 lx (comparable to the full Moon on a dark street without streetlights). Light intensities were measured using a light meter (Dr. Meter, support@drmeter.com) inside the goggles, and room light intensities were monitored between trials to ensure

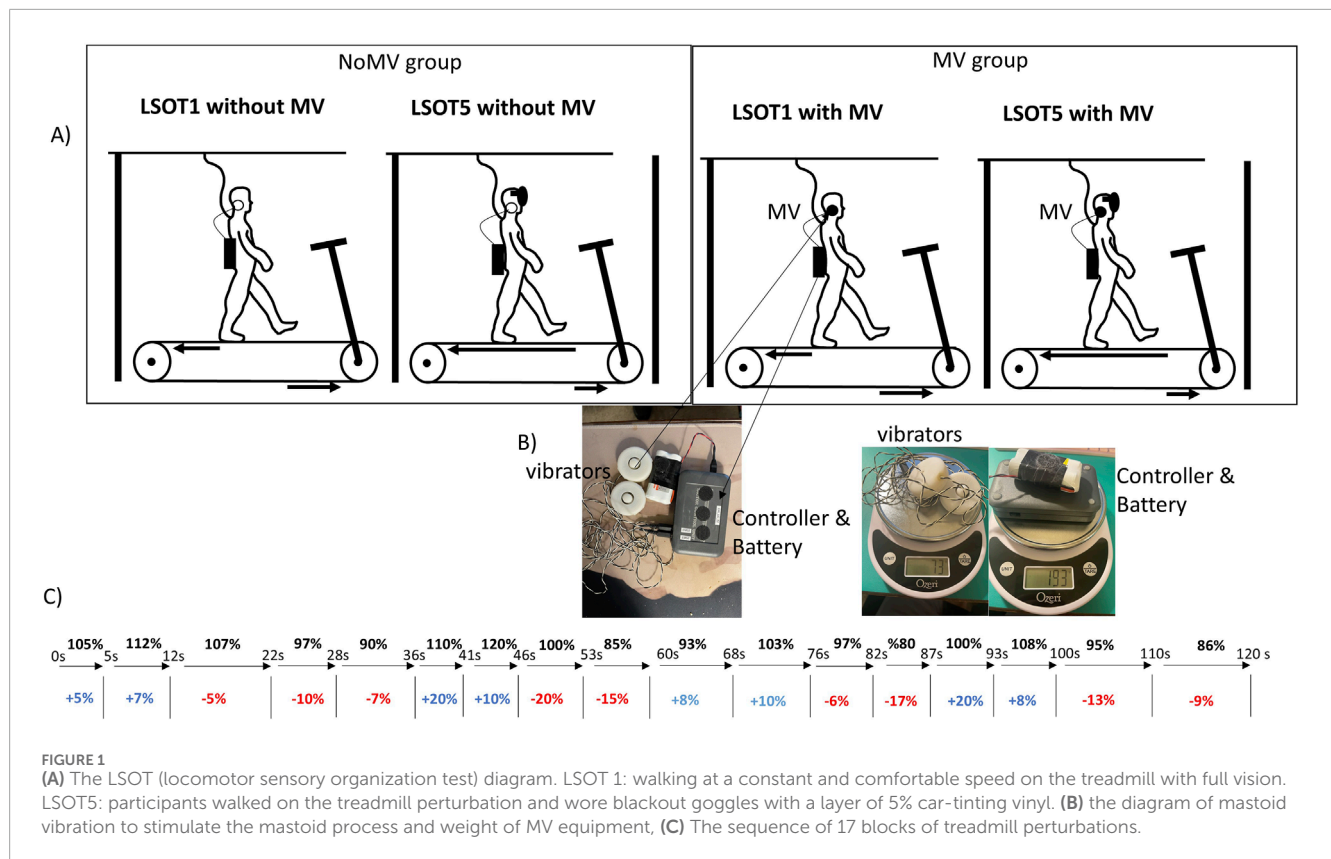


FIGURE 1
(A) The LSOT (locomotor sensory organization test) diagram. LSOT 1: walking at a constant and comfortable speed on the treadmill with full vision. LSOT5: participants walked on the treadmill perturbation and wore blackout goggles with a layer of 5% car-tinting vinyl. **(B)** the diagram of mastoid vibration to stimulate the mastoid process and weight of MV equipment, **(C)** The sequence of 17 blocks of treadmill perturbations.

consistency throughout data collection. For the Mastoid Vibration (MV) group, the bilateral mastoid vibrations were generated by two electromechanical vibrotactile transducers (EMS2 tactors; Engineering Acoustics, Casselberry, FL, USA; see [Figure 1](#)). These transducers were affixed inside a customized swim cap using double-sided adhesive strips and could be adjusted to position them on the mastoid processes bilaterally. Designed for mounting with a cushion, they could produce high displacement levels, enabling the vibration to be easily sensed even through layers of padding. The controller and battery weighed 193 g and two vibrators weighed 73g, so total weight of this MV equipment was 266 g ([Figure 1](#)). A frequency of 100 Hz was chosen for bilateral mastoid process stimulation as it has been demonstrated to trigger nystagmus and necessitate compensatory responses from the vestibular system in healthy young adults ([Perez, 2003](#)), patients with vestibular neuritis ([Nuti and Mandalà, 2005](#)), and patients with otosclerosis ([Manzari et al., 2008](#)). The amplitude of supra-threshold vibrations was set at 130% of the amplitude perceivable by the participants ([Lu et al., 2022](#)). The frequency and amplitude of the mastoid vibrations were controlled by software (TAction Creator; Engineering Acoustics, Casselberry, FL, USA) by transmitting the designed signal from the laptop to the controller via Bluetooth technology. The minimum perceived amplitude was determined by adjusting the vibration amplitude through the TAction Creator commercial software until participants could perceive it while standing. The vibrations were administered to participants on both mastoid processes simultaneously. The vibration activation followed an impulse-type pattern, with a 0.5 s activation period and a 0.5 s deactivation period ([Lu et al., 2022](#)).

The rationale for using this impulse-type vibration was to mitigate the saturation of the vestibular sensation ([Chien et al., 2016](#)).

2.3 Experimental protocol

After participants voluntarily signed the informed consent, PWS needed to be obtained. For both groups, the experimenters increased the treadmill speed to 0.8 m/s and instructed participants to step on the belt. After 20 s, participants were asked whether this speed was comfortable, like walking around the neighborhood. The speed was increased or decreased by 0.1 m/s based on participants' responses by experimenters. This procedure was performed repeatedly until the participants confirmed the PWS. Once the PWS was identified, the participants walked on the treadmill for 5 minutes to familiarize themselves with treadmill walking. After familiarization with treadmill walking, participants took a 2-min mandatory rest. Then, participants were randomly assigned into two groups: NoMV and MV groups. Next, two conditions (LSOT1 and LSOT5) will be assigned randomly to these participants. For the NoMV group, participants walked in LSOT1 and LSOT5 without any mastoid vibration. Conversely, for the MV group, participants walked in LSOT1 and LSOT5 with bilateral mastoid vibrations. It should be noted that both MV and control groups wear this MV equipment (two transducers were attached on two sides of mastoid process, and a control attached on around location of sacrum). Also, the mixed experimental design (within group: LSOT1 vs. LSOT5; between groups: the effect of mastoid vibration) was implemented according to previous published study ([Wang et al., 2024](#)). [Wang et al. \(2024\)](#)

investigates the margin of stability when walking on similar LSOT conditions (LSOT1, LSOT4, and LSOT5) similar to the present study by using a single group and find an apparent limitation—the learning effect between similar conditions although a 2-min mandatory rest between conditions is provided to participants. They wrote “the limitation was whether a 2-min rest was enough to eliminate the learning effect. This present study did not provide sufficient, direct evidence to support this claim.” In the current study, if the same participants were assigned to walk two LSOT5, the potential learning effect may be inevitable. Thus, in this current study, a mixed experimental was used. Also, each participant only experience LSOT5 one time. All participants wore the MV device, but the MV only was applied in the MV group. In LSOT5, the sequence of blocks was presented in the same order to each participant to ensure that the outcomes remained comparable both within and between groups. Also, between conditions, a 2-min mandatory rest was assigned to participants to catch their breath. Each LSOT condition lasted 2 minutes. Thus, two 2-min LSOT conditions (one LSOT1 and one LSOT5) were assigned to each participant. At the end of each trial, the participants were instructed to sit on a chair with handles. They were asked if they felt uncomfortable sensations like nausea, vomiting, or dizziness. If participants experienced any discomfort, the experiment was immediately terminated. Also, each participant was asked to verbally describe their experience while walking after each condition.

2.4 Data analysis

The GRF were analyzed along the vertical (V), anterior-posterior (AP), and medial-lateral (ML) directions. Initially, the raw GRF data from the instrumented treadmill were filtered using a fourth-order low-pass Butterworth filter with a 10 Hz cut-off frequency (McCaw et al., 2013). The GRF components in each direction were reported for peaks V1, AP1, ML1, and V2, AP2, and ML2 (Figure 2). All GRFs were normalized with respect to each participant's body weight (McCaw et al., 2013). The GRF was utilized to discern a crucial gait event—initial heel contact. The initial heel contact was determined as the instant when the vertical component of the ground reaction force exceeded 10 N and was sustained for 40 ms (Chien et al., 2014). A stance cycle represented the duration between two consecutive initial heel contacts for each leg. The GRF variability was defined as the coefficient of variation of each dependent variable within the gait cycles observed over a period of 2 minutes for each trial.

2.5 Statistical analysis

The dizziness handicap score was not included in the statistical analysis here because participants with a score greater than zero were excluded from the study.

A Shapiro-Wilk normality test with an alpha value of 0.05 was used to evaluate the normality for each dependent variable and participants' information. All data were analyzed using SPSS (26.0).

- If the participants' information were normally distributed, the independent t-test was used; otherwise, the Mann-Whitney Test was used.
- If the data were normally distributed, a mixed two-way repeated measure ANOVA (2 LSOT conditions x mastoid vibration) was used to investigate the condition effect and mastoid vibration effect as well as the interaction between these two effects. If a significant interaction was found, pairwise comparisons were corrected by the Bonferroni method. An independent t-test was used to compare between groups and a pair t-test was used to compare means within conditions.
- If the data were not normally distributed, Friedman's two-way analysis of variance by ranks was used. If the Friedman test showed significance the Mann-Whitney Test was used to compare means between groups (e.g., LSOT1 vs. LSOT1MV) and the Wilcoxon Signed Ranks Test was used to compare means from a same group in different conditions (LSOT1 and LSOT5).
- It should be noted that the Bonferroni corrections were applied in all pairwise comparisons ($6 \times 12 = 72$, as there were 12 variables); therefore, the significant level was $0.05/72 = 0.0007$. The alpha value needed to be smaller than 0.0007 to be significant.

The effect size was calculated using partial eta squared values for normal distribution data (small effect: 0.01, medium effect: 0.06, large effect: 0.14) and using Kendalls W values for non-normal distribution data (small effect: 0.1, medium effect: 0.3, large effect: 0.5). All criteria for identifying the effect size using Cohen's interpretation guidelines (Cohen, 1988).

3 Results

3.1 Participants' information between two groups (NoMV and MV groups)

There were no significant differences in age ($p = 0.072$), height ($p = 0.576$), weight ($p = 0.750$), and preferred walking speed ($p = 0.425$). More details are shown in Table 1.

3.2 Normalized test

The Shapiro-Wilk normality test showed that.

- Normally distribution in AP1, ML1, ML2.
- Non-Normally distribution in V1, V1V, V2, V2V, AP1V, AP2, AP2V, ML1V, ML2V.

3.3 Effects of LSOT conditions and bilateral mastoid vibrations

- A two-way mixed ANOVA repeated measure was used to investigate whether AP1, ML1, and ML2 differed in different

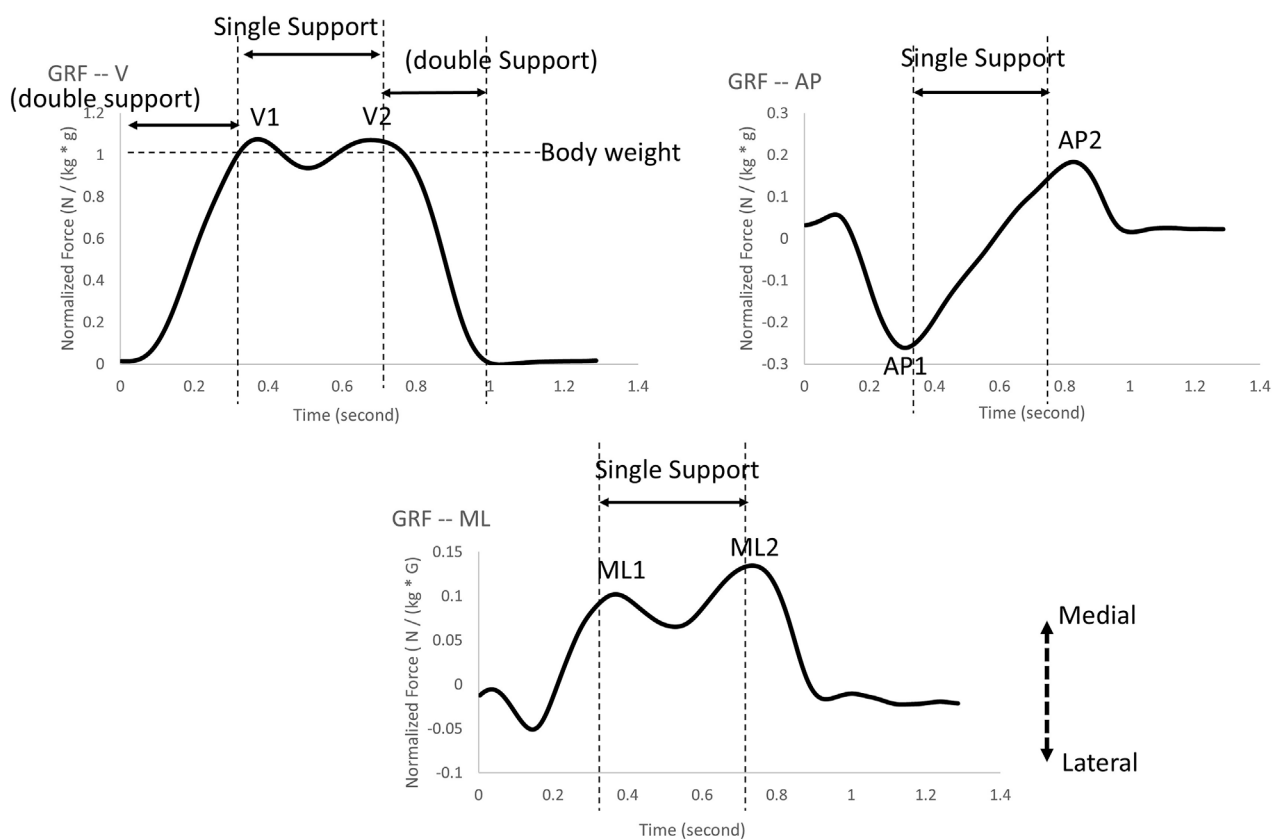


FIGURE 2

The ground reaction force peaks were selected in the present study: V1 and V2 represent ground reaction force peaks in the vertical direction; AP1 and AP2 represent ground reaction force peaks in the anterior-posterior direction; ML1 and ML2 represent ground reaction force peaks in the medial-lateral direction.

LSOT conditions with/without bilateral MV. A significant interaction was found in aforementioned variables (AP1: $F_{1,58} = 22.905, p < 0.0001$; ML1: $F_{1,58} = 6.588, p = 0.013$; ML2: $F_{1,58} = 11.544, p = 0.001$).

- Friedman test was conducted to determine whether each dependent variable differed in different LSOT conditions with/without bilateral mastoid vibrations. A significant difference was found in V1 ($\chi^2(3) = 72.6, p < 0.001$), VV1 ($\chi^2(3) = 40.92, p < 0.001$), V2 ($\chi^2(3) = 52.56, p < 0.001$), VV2 ($\chi^2(3) = 62.96, p < 0.001$), APV1 ($\chi^2(3) = 58.08, p < 0.001$), AP2 ($\chi^2(3) = 34.6, p < 0.001$), AP2V ($\chi^2(3) = 64.52, p < 0.001$), ML1V ($\chi^2(3) = 34.68, p < 0.001$), and ML2V ($\chi^2(3) = 35.08, p < 0.001$).

The means, medians, and standard deviations are shown in Table 2. The pairwise comparisons are shown in Table 3, Figures 3–8.

3.4 The size effect

The partial eta squared values were 0.283 for AP1, 0.102 for ML1, and 0.187 for ML2. The Kendalls W values were 0.807 for V1, 0.455 for V1V, 0.584 for V2, 0.7 for V2V,

0.645 for AP1V, 0.384 for AP2, 0.717 for AP2V, 0.385 for ML1V, and 0.39 for ML2V. These values supported that the effect size of this study was from medium to large effect.

4 Discussions

Studying the ground reaction force (GRF) while walking under vestibular-demanding conditions (LSOT1) with or without mastoid vibrations (MV) aimed to elucidate how humans redistribute forces compared to normal walking (LSOT1) with or without MV. This study confirmed the hypotheses that 1) walking in LSOT5 increased the GRF variabilities in V and AP directions, 2) walking with MV decreased the GRFs in V and AP directions; and 3) walking in LSOT5 with MV increased the GRF variability most compared to walking in LSOT1 without MV, indicating that LSOT5 can be used to identify the deteriorations in vestibular system. The results rejected our hypotheses that 1) walking in LSOT five did not affect the GRFs compared to walking in LSOT1 with/without MV; and 2) there was no effect of LSOT conditions or the effect of MV on GRFs in ML directions.

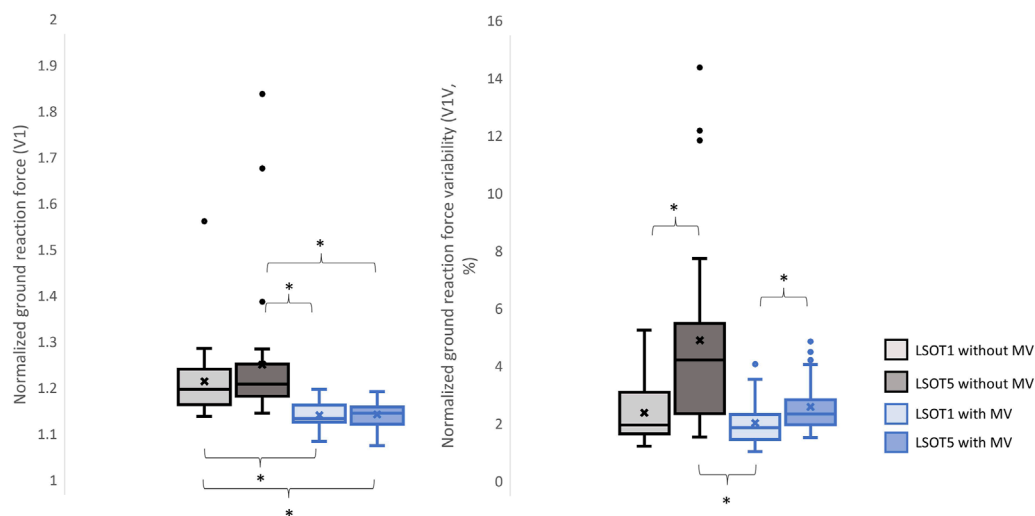


FIGURE 3
The normalized GRF V1 and respective variabilities, V1V, *: $p < 0.0007$.

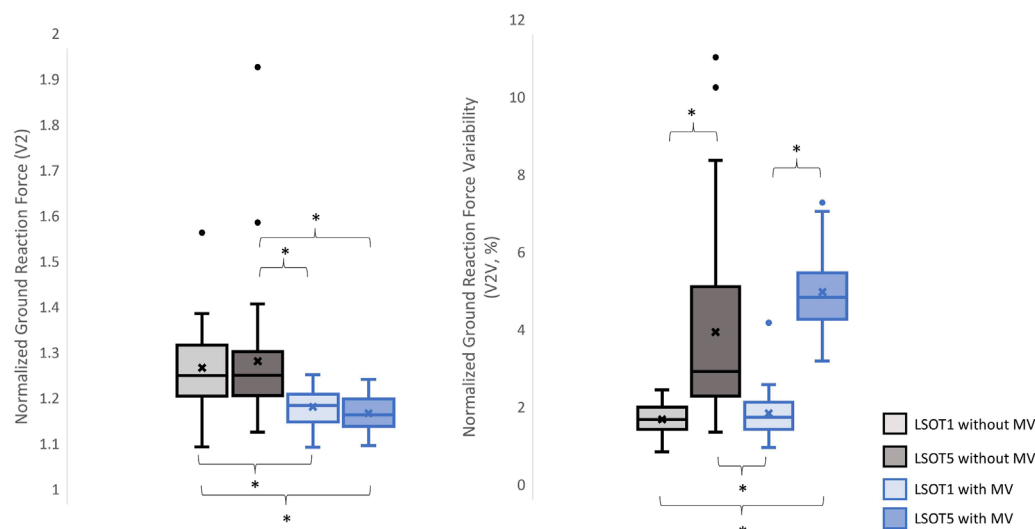


FIGURE 4
The normalized GRF V2 and respective variabilities, V2V, *: $p < 0.0007$.

4.1 Walking in the vestibular-demanding task (LSOT5) necessitated adjustments in GRF from one stance cycle to another, irrespective of whether mastoid vibrations were administered

It has been demonstrated that various forms of vestibular stimulation significantly influence the margin of stability variability in both the anterior-posterior and medial-lateral directions in young adults (Lu et al., 2022). Additionally, simply walking blindfolded has been shown to increase step length variability (Bauby and Kuo, 2000), while walking on an oscillating surface increases trunk variability in both the anterior-posterior and

medial-lateral directions (McAndrew et al., 2010). Moreover, studies have indicated that walking in LSOT5 increases net center of pressure sway variability compared to walking in LSOT1 (Chien et al., 2014). These findings collectively suggest that less reliable sensory systems may result in greater variability. The present study observed significant increases in GRF variabilities in the V and AP directions when walking in LSOT5 compared to LSOT1 regardless of whether the MV was administered (V2: 2.23 (LSOT1) vs. 5.36 (LSOT5), an increase in 140.35%; AP2: 10.89 (LSOT1) vs. 17.03 (LSOT5), an increase in 56.38%) or not (V2: 2.07 (LSOT1) vs. 4.33 (LSOT5), an increase in 109.17%; AP2: 8.21 (LSOT1) vs. 15.32 (LSOT5), an increase in 86.60%). This observation may be explained by the concept of the internal

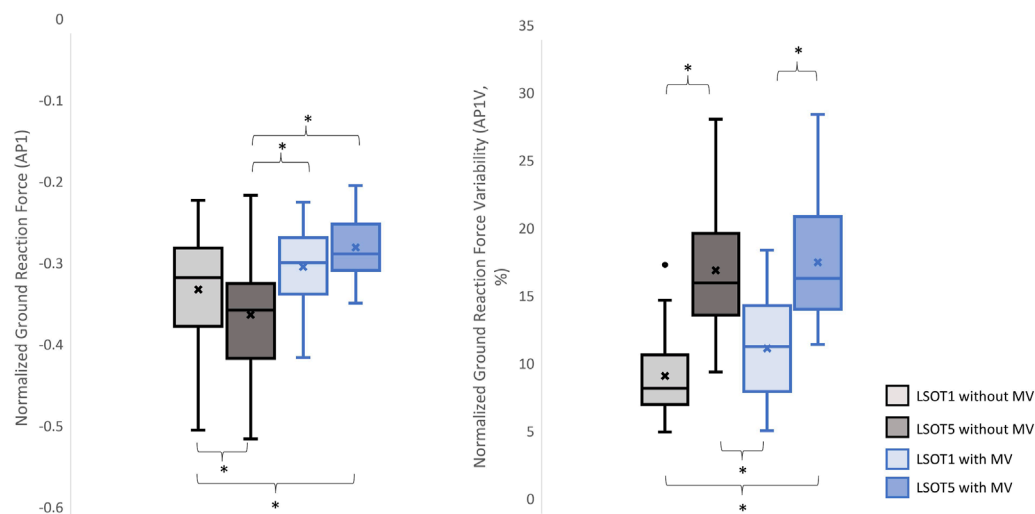


FIGURE 5
The normalized GRF AP1 and respective variabilities, AP1V,*: $p < 0.0007$.

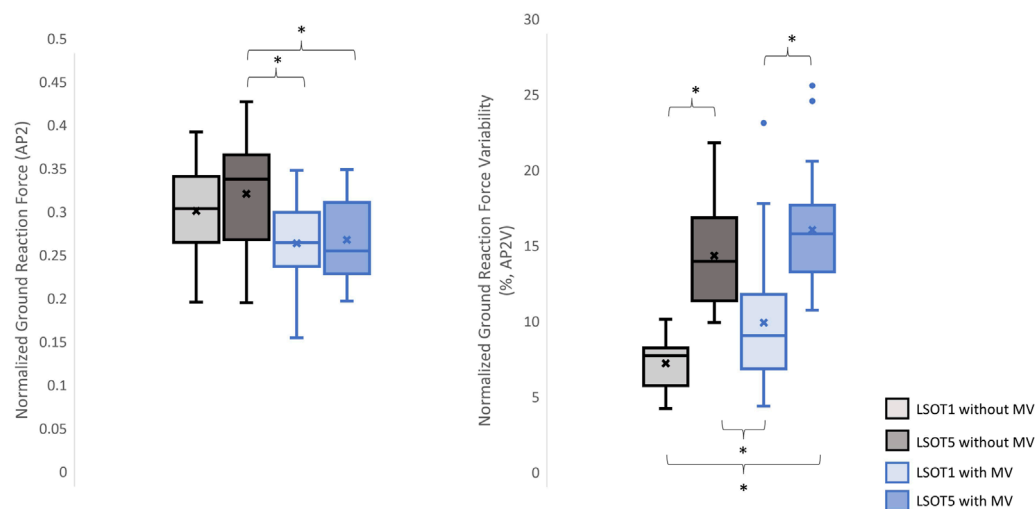


FIGURE 6
The normalized GRF AP2 and respective variabilities, AP2V,*: $p < 0.0007$.

model (Merfeld et al., 1999), which refers to the brain's ability to store information about the external environment related to the individual's surroundings. According to Ito (2008), the internal model of stability control consists of several major components, including the instructor (prefrontal cortex), the controller (motor cortex), the controlled object (body parts), the sensory systems (visual, somatosensory, vestibular systems), and the internal model itself (forward or inverse model). During walking in LSOT5, where participants were navigating an unfamiliar condition, the instructor (prefrontal cortex) initially receives environmental information primarily from the vestibular system, with a lesser reliance on the visual and somatosensory systems. Subsequently, the instructor provides instructions to

the controller (motor cortex), sending motor commands to the controlled objects to maintain stability. Concurrently, the controller sends a signal back to the internal model to compare the actual body position with the predicted position based on the forward model. If disparities between the predicted and actual body positions are detected, the internal model may correct these differences and transmit the corrections back to the instructor. This iterative process of correction is likely repeated to counteract unpredictable sensory conflicts from the visual and somatosensory systems during walking in LSOT5. Consequently, these continual corrections may lead to stride-to-stride adjustments, resulting in greater GRF variability in LSOT5 compared to LSOT1.

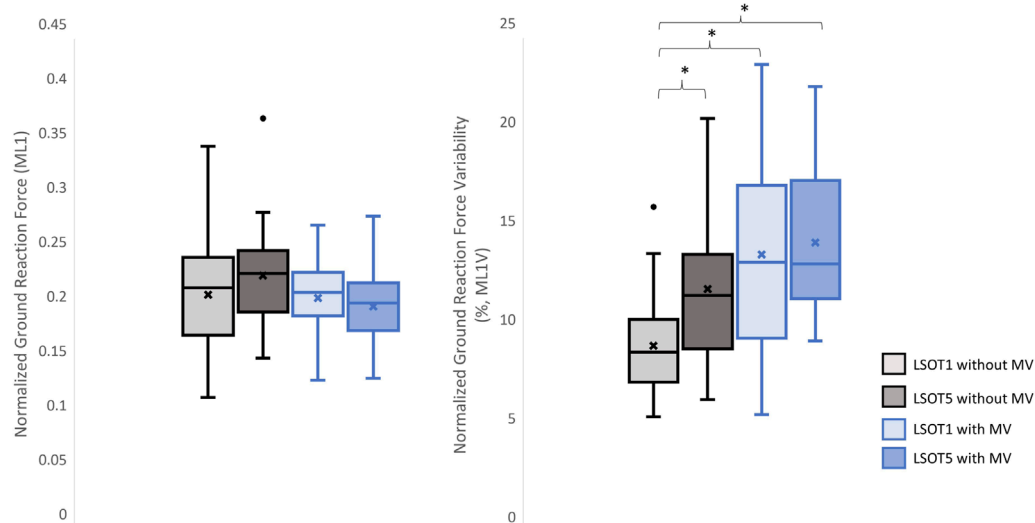


FIGURE 7
The normalized GRF ML1 and respective variabilities, ML1V, *: $p < 0.0007$.

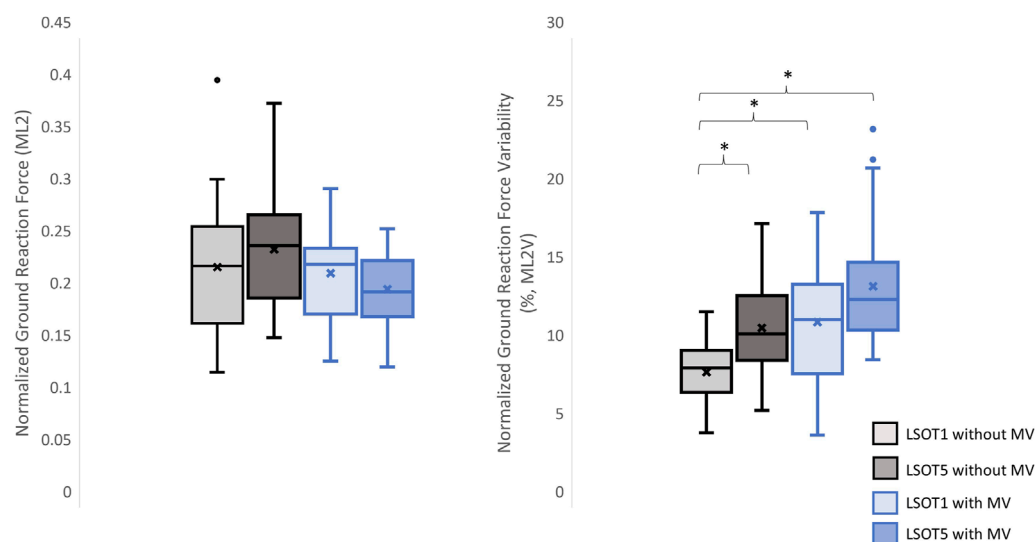


FIGURE 8
The normalized GRF ML2 and respective variabilities, ML2V, *: $p < 0.0007$.

It was worth mentioning that the significant differences in GRFs between LSOT one and LSOT five regardless of whether MV was administrated or not were not found in this study. It might be the experimental design that the mean of treadmill was 99.3% of the preferred walking speed in LSOT5, which was very close to the preferred walking speed in LSOT1. It has been shown that the amplitudes of GRFs are highly correlated to the walking speed (Nilsson and Thorstensson, 1989); therefore, it may be a possibility that the GRFs was averaged out as a result of step-by-step adjustments (greater GRF variabilities) associated with slowed-down and sped-up treadmill settings in LSOT5.

4.2 Walking with bilateral mastoid vibrations reduced the peaks of GRF

First and foremost, mastoid vibration (MV) at a stimulation frequency of 100 Hz has been utilized for decades to assess various types of vestibular disorders, including unilateral vestibular loss (Lucke, 1973), unilateral vestibular lesions (Dumas et al., 2007), partial unilateral vestibular lesions (Dumas et al., 2011), vestibular neuritis (Karlberg et al., 2003), and superior semicircular canal dehiscence (Dumas et al., 2014). The aforementioned studies have employed vibration-induced nystagmus, an abnormal eye movement, to gauge the efficacy of MV in diagnosing these diverse

forms of vestibular disorders. For example, in individuals with partial or total unilateral vestibular lesions, stimulating both sides of the mastoid process results in vibration-induced nystagmus shifting away from the affected side (Lucke, 1973; Yagi and Ohyama, 1996; Hamann and Schuster, 1999; Karlberg et al., 2003; Dumas et al., 2007). Conversely, in patients with superior semicircular canal dehiscence (Dumas et al., 2014), vibration-induced nystagmus shift toward the side of the lesion when MV is applied. Interestingly, when individuals with bilateral areflexia and symmetrical hypofunction stimulate both sides of the mastoid process, no changes in vibration-induced nystagmus are observed (Dumas et al., 2011; Dumas et al., 2014). Moreover, Kavounoudias et al. (1999) applied vibration to the mastoid process and observed that the body moved toward the opposite direction from where the vibration was applied unilaterally. When two skull vibrators were positioned perpendicular to each other, the body moved diagonally, and when placed on both sides of the head in similar locations, the body moved forward. Kavounoudias et al. (1999) suggested that vibrations induced vestibular-proprioceptive processing and generated the vestibular illusion. For instance, when vibration activated the dorsal neck muscles, a proprioceptive signal suggested that the head was inclined forward relative to the trunk, while the vestibular signal indicated that the head remained straight. Consequently, the forward-directed postural sway induced by this dorsal neck vibration is likely a compensatory response aimed at restoring the body to an upright position. Similar observations were found in Chien et al., 2016; Chien et al., 2017, where walking in LSOT5 with bilateral MV significantly increased the degree of freedom of net center pressure movement in the AP direction compared to walking in LSOT5 without MV in both young and older adults. In the present study, applying bilateral mastoid vibrations might have generated the aforementioned vestibular illusion, causing the body to continuously move forward during treadmill walking and further increase the cadence (Dakin et al., 2013; Sun et al., 2023). Increased cadence resulted in reduced GRF peaks (Musgjerd et al., 2021). Thus, this might be why the reductions in GRFs with MV than without MV in V (V1: 1.25 of body weight (LSOT1) vs. 1.17 of body weight (LSOT1MV), a decrease in 6.4%; V1: 1.28 of body weight (LSOT5) vs. 1.17 of body weight (LSOT5MV), a decrease in 8.59%; V2: 1.29 of body weight (LSOT1) vs. 1.21 of body weight (LSOT1MV), a decrease in 6.2%; V2: 1.31 of body weight (LSOT5) vs. 1.2 of body weight (LSOT5MV), a decrease in 8.39%) and AP directions (AP1: 0.35 of body weight (LSOT5) vs. 0.26 of body weight (LSOT5MV), a decrease in 25.71%; AP2: 0.34 of body weight (LSOT5) vs. 0.28 of body weight (LSOT5MV), a decrease in 17.64%) were observed in the present study.

4.3 Walking in LSOT5 with bilateral mastoid vibration posed a greater challenge

In the present study, the lowest amplitudes of GRFs were observed in V1 (1.17 of body weight), V2 (1.2 of body weight), AP1 (0.26 of body weight), ML1 (0.20 of body weight), and ML2 (0.21 of body weight), while the highest variabilities were found in V2V (5.37), AP1V (18.58), AP2V (17.03), ML1V (14.66), and ML2V (14.17) when walking in LSOT5 with mastoid vibrations compared to walking in LSOT1 without mastoid vibrations (V1:

1.24, V2: 1.29, AP1: 0.31, ML1: 0.22, ML2: 0.23 of body weight; V2V: 2.07, AP1V: 10.19, AP2V: 8.21, ML1V: 9.44, ML2V: 8.67). It was noted that greater negative values indicated greater GRF in the AP. These changes are likely attributed to walking in a vestibular-demanding environment and the vestibular system was disrupted or deteriorated. This observation aligned with Wood et al.'s (2015), which applied SOT5 to measure vestibular function in 37 astronauts upon returning to Earth's surface, revealing an 82.4% increase in sway post-spaceflight compared to pre-flight, indicating significant vestibular deterioration in microgravity. Mulavara et al. (2010) designed a functional mobility test to assess locomotor function post-spaceflight, including passing through vertical pylons, a gate, and a couple of obstacles. The surface was built with a compliant foam surface to "make the support surface unreliable," similar to LSOT5's design, inducing sudden acceleration/deceleration in the AP direction. They found that astronauts who spent 163–195 days in the International Space Station took double the time to complete this functional mobility test upon landing, suggesting sensory system deterioration, particularly in the vestibular function. The findings of our study (the significant differences in GRF between with and without MV when walking in LSOT5) have dual implications: firstly, walking under LSOT5 could potentially differentiate vestibular status across various scenarios using GRF measure, such as pre- and post-spaceflight or pre- and post-landing in different gravity levels, and may indicate the duration required for full vestibular system recovery after returning from space. Secondly, training in walking under LSOT5 with mastoid vibration could enhance locomotor adaptation capabilities in sensory-conflicted situations. Previous research has demonstrated that treadmill-induced perturbation training improves balance and reduces fall risk in older adults (Kurz et al., 2016), suggesting that incorporating LSOT5 with mastoid vibration into future sensorimotor training protocols may enhance sensory integration capabilities in astronauts navigating unpredictable environments, such as quicksand on a dark night under varying gravity levels.

4.4 Why did walking with/without mastoid vibration have no effect on the mean GRFs but increase the GRF variabilities in the ML directions?

Unexpectedly, no significant differences in GRFs in the ML direction was observed when walking with or without MV. Bauby and Kuo's study (2000) suggested that active control in the ML direction was heavily necessary when walking blindfolded (actively controlled) by measuring their step width variability. McGeer (1990) demonstrated that a bipedal robot without any control mechanism could mimic human-like gait in the AP direction while walking downhill. However, this robot was prone to falling sideways due to the lack of a control mechanism, supporting the active control hypothesis. Additionally, research has indicated that walking on sinusoidal surface oscillations in the anterior-posterior (AP) direction impacts the margin of stability in the medial-lateral (ML) directions (McAndrew-Young et al., 2012). A study even demonstrated that walking in vestibular-demanding tasks, such as narrow walking with galvanic vestibular stimulation, requires active control in the ML direction, as evidenced by increased GRF

peak amplitudes in the ML direction and muscle activations in the erector spinae (Magnani et al., 2021). These findings contradicted the results of the present study, which found that treadmill-induced perturbations in the AP direction did not affect the GRF peaks in the ML directions. A possible rationale to explain the no significant observations on mean GRFs in the present study was that the changes in GRFs in the ML direction were averaged out due to the mean treadmill speed was similar within the LSOT conditions (LSOT1: 100% of PWS, and LSOT5: 99.29% of PWS) and between the groups. Research has demonstrated a negative linear correlation between step width and walking speed when walking at 80%–120% of preferred walking speed (Brinkerhoff et al., 2023). Therefore, in LSOT5, after averaging the walking speed over 17 types of treadmill-induced perturbations (mixed acceleration and deceleration of the treadmill speed), the changes in gait characteristics, which influenced the GRF, in the ML direction should be similar to those observed in LSOT1, regardless of whether MV was administered or not. Hu and Chien (2021) confirmed this hypothesis, demonstrating that the step width while walking in the LSOT5 (12.35 cm) were similar to those observed in the LSOT1 (12.18 cm). In contrast, a significantly GRF variability in the ML direction and step width variability were noted in the previous (Hu and Chien, 2021) and current study. This GRF variability, step-to-step adjustment, can be attributed to the foot placement strategy, which regulated the location of foot placement at the moment of heel contact as needed. By effectively positioning the center of pressure mediolaterally in relation to the center of mass, the GRF generates a moment that helps prevent falls (van Leeuwen et al., 2020). Furthermore, the step-by-step foot placement was influenced by the activity of the hip abductor and adductor muscles during steady-state walking (hip strategy, van Leeuwen et al., 2020). It has been shown that walking in LSOT5 necessitated step-to-step adjustments in the ML direction compared to walking in LSOT1, as evidenced by the 95% confidence ellipse area of foot placement distribution (Hu and Chien, 2021). Specifically, their investigation revealed that the length of the short axis of the ellipse in the ML direction increased by 25.65%, from 33.96 mm (LSOT1) to 42.67 mm (LSOT5), while the length of the long axis (AP direction) increased by 55.47%, from 64.34 mm to 100.05 mm in healthy young adults. In the current study, the greater GRF variability necessitated larger step-to-step adjustments when walking in LSOT5 without MV, in LSOT1 with MV, or in LSOT5 with MV compared to walking in LSOT1 without MV. This finding indicated that step-to-step adjustments were essential, suggesting that whenever engaging in vestibular-demanding tasks or under conditions that disrupt the vestibular system, active control in a step-to-step manner in the ML direction was highly demanded. Although the hip strategy could not be measured in this study due to the absence of a motion capture system, it was likely speculated that the hip strategy would be utilized while walking in LSOT5, regardless of whether MV was administered. Furthermore, when the bilateral MV was applied and walking in LSOT5, these participants may have had no choice but to primarily use the hip strategy to actively adjust their step-to-step foot placement.

4.5 Conclusions and limitations

Several limitations warrant consideration for future studies.

- This study focused exclusively on young adults, and future research should encompass astronauts both pre- and post-spaceflight to enhance applicability.
- Walking speed was not controlled, as imposing a fixed speed among participants might alter participants' natural gait patterns. Consequently, variations in stance cycles across participants and trials could potentially influence the means and variability of GRF peaks. Thus, the coefficient of variation was utilized as the variability measure to mitigate this limitation.
- The absence of joint angle, head, and trunk movement tracking may have limited the ability to directly elucidate the effects of visual manipulations and treadmill-induced perturbations on the vestibular system and the applied strategies, such as hip and ankle strategies during walking. Future investigations should include joint angle, head and trunk movements tracking to address this limitation.
- The impulse of GRFs in each direction comprises two components: GRFs and time duration. Hence, the duration of each stance phase may vary among participants. Additionally, the number of stance phases may differ between participants and even within the same individual across different conditions. Consequently, the analysis of GRF impulse parameters was excluded at the present time.
- The impact of spacesuits on gait patterns should also be considered in future studies.

In summary, this pioneering study underscores the distinct responses of ground reaction force and its variabilities to different sensory challenges during walking. This paradigm may shed light on potentially assessing vestibular function during walking and aiding sensorimotor adaptation in future space missions.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary Material](#), further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Nebraska Medical Center Institutional Review Board (IRB# 340-10-FB). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ZW: Conceptualization, Formal Analysis, Funding acquisition, Methodology, Writing—original draft, Writing—review and editing. HX: Conceptualization, Formal Analysis, Methodology, Writing—original draft, Writing—review and editing. JC: Conceptualization, Data curation, Formal Analysis, Funding

acquisition, Investigation, Methodology, Project administration, Software, Writing–original draft, Writing–review and editing.

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at the Department of Health and Rehabilitation Science, College of Allied Health Professions, the University of Nebraska Medical Center, Omaha, Nebraska, USA, when Zhuo Wang and Haoyu Xie were graduate students in the USA.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fphys.2024.1325513/full#supplementary-material>

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Echocardiography screening of German military pilot applicants as an example for high-hazard occupations

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Introduction: Pre-employment screening is of utmost importance in high-risk occupations for the early diagnosis and prevention of cardiac and non-cardiac disease, and for risk mitigation. Recommendations for echocardiography screening, however, are contradictory. It was the aim of this study to retrospectively analyze echocardiography data from German military pilot applicant screening to find out in how many cases cardiac disease was diagnosed, and how often the diagnosis influenced aeromedical decision making.

Methods: 6,110 screening echocardiographies from German military pilot applicants, 5,923 were male, examined between January 2007 and June 2020 were retrospectively analyzed for findings and their impact on aeromedical decisions.

Results: During a 14.5-year period, 4,477 out of 6,110 screening echocardiograms were normal. The remaining 1,633 applicants revealed a total of 1,962 abnormalities, mainly consisting of minor tricuspid and mitral valve regurgitations (81.9%). Due to echocardiography findings, 80 applicants (1.3%) were unfit for flying duties, 9 (0.1%) were fit with limitations, and 1,544 (25.3%) were fit with findings that had to be monitored over time, but which were not aeromedically relevant. The most common diagnoses leading to disqualification or limitations were bicuspid aortic valve with or without aortic regurgitation (84.9%) and mitral valve prolapse with or without regurgitation (9.3%).

Conclusion: Percentages of abnormal findings were similar to other studies. Aeromedical assessments based on those findings, however, were slightly different, as they depend on national employment policies. As a consequence, the usefulness of echocardiography may vary between different countries and different professions, depending on the acceptance of certain findings for employment.

KEYWORDS

pre-employment screening, echocardiography, pilot applicant, high-risk occupation, aeromedical assessment, military

Introduction

High-hazard occupations require optimal health in the workforce to mitigate the risk of incapacitation and distraction and so to reduce safety risks to themselves, other employees, and the general public (1). These professions include pilots, astronauts, divers, mountaineers, offshore workers, emergency workers (firefighters, emergency healthcare workers, law enforcement

personnel), and professional drivers. For example, there have been a number of aircraft incidents and accidents, some of them with fatalities, that were directly caused by myocardial infarctions of the pilots flying (2).

Pre-employment screening and periodic medical examinations in accordance with national and international laws and regulations are of utmost importance for those high-risk occupations for the early diagnosis and prevention of cardiac and non-cardiac disease, and for risk mitigation. The early recognition of health problems is especially important for first applicants, as they may spend their whole career in a high-risk profession. A premature end of their career because of a disease should be prevented as well as an aggravation of an undetected disease by the exercise of their profession.

Cardiovascular disease is one of the most common medical reasons for incapacitation or distraction of high-hazard employees (3, 4). Therefore, a variety of cardiovascular screening recommendations exists for different professions, e. g. regarding screening by electrocardiography or exercise electrocardiography (5–7). Recommendations for echocardiography screening, however, are contradictory, although the diagnosis of many cardiac diseases and abnormalities is not possible without echocardiography or more sophisticated cardiac imaging (8).

The air forces of some allied countries including the US Air Force do not perform echocardiography screening in pilot applicants, because the number of abnormal findings in the specific age group, most applicants are aged from 18 to 25 years, is low, and echocardiography screening is therefore deemed to be not efficacious (9). A different attitude is shared by the air forces of other countries including Germany, which routinely perform echocardiography screening in pilot applicants, based on the assumption that certain abnormal findings are of such importance for aeromedical assessment that echocardiography screening is justified.

Among the group of high-hazard occupations, pilots are very intensely regulated by a variety of medical standards issued by national and international organizations and licensing authorities (10). Pilot screening can therefore be used as an example for other high-risk occupations.

The aim of this study is to retrospectively analyze echocardiography data from German military pilot applicant screening in order to find out in how many cases cardiac disease has been diagnosed, and how often the diagnosis has influenced aeromedical decision making.

The study has to be seen in the context of an intended harmonization and possibly standardization of screening programs among allied countries. Recently, a North Atlantic Treaty Organization (NATO) working group (Human Factors and Medicine (HFM) 386) has been initiated as a three-year project, titled “Cardiac Screening on Military Aircrew and Other High Demand Military Personnel” and working on these questions.

Materials and methods

The digital information system (DIL 2006, Noris Ingenieurbüro GmbH, Nürnberg, Germany) of the German Air Force Centre of Aerospace Medicine was searched for pilot applicant screening from January 1, 2007, to June 30, 2020. All echocardiography results were retrospectively analyzed, age, height, weight, and body mass index were also captured. If the digital documentation was not conclusive, the original paper documentation was screened for additional information. Most applicants were civilians, a minority was already part of the armed forces, air force, army, or navy, and was performing

other duties. All applicants were pre-selected in an assessment center including a simple medical screening not including echocardiography. All applicants for flying duties independently of their future branch (air force, army, navy) or their future aircraft type (high-performance aircraft, fixed-wing aircraft, rotor-wing aircraft, drones) are screened in the German Air Force Centre of Aerospace Medicine for the German Armed Forces (Bundeswehr).

In total, 6,609 examinations were performed during the analyzed period. Out of these, 31 were excluded, because the same person was examined twice. In these cases, only the first screening echocardiography was included in the study. Six additional examinations were excluded, because the applicants were examined twice, and only in the second examination a screening echocardiography was carried out. Only this second examination was included in the study. So, in total, 6,572 examinations from different applicants could be used. Out of these, 444 examinations (6.8%) had to be excluded, because no echocardiography screening was performed. An additional 18 examinations (0.3%) were excluded, because the echocardiography diagnosis was not usable, as both the digital and the original paper documentation were not meaningful. This means that 6,110 echocardiograms could be included in this study (92.3% of all applicants screened during this period of time), 5,923 (96.9%) were males and 187 (3.1%) were females. The average age of the applicants was 21.1 ± 3.3 [95%-Confidence interval (CI): 21.0–21.2] years (min: 16.4 years, max: 52 years), the body height was 180.3 ± 6.7 cm (95%-CI: 180.1–180.5 cm; min: 155.1 cm, max: 204.0 cm), the body weight 75.7 ± 9.9 kg (95%-CI: 75.4–75.9 kg; min: 50.3 kg, max: 121.4 kg), and the body mass index (BMI) was 23.3 ± 2.5 kg/m² (95%-CI: 23.2–23.3 kg/m²; min: 16.7 kg/m², max: 35.5 kg/m²).

Echocardiographies were performed with Vivid 7 and Vivid E9 by GE HealthCare Technologies, Inc., Chicago, IL, United States. All examinations were performed by physicians with special training in echocardiography. As minimum requirements the examinations consisted of two-dimensional echocardiography, color doppler, pulsed wave doppler, and continuous wave doppler. Three-dimensional echocardiography or tissue doppler were added on indication. Standard views were left parasternal views (long and short axis) and left apical views (four-chamber, five-chamber, two-chamber, three-chamber). Right parasternal and apical view, suprasternal, and subcostal views were added on indication. Assessments and measurements were performed in accordance with current guidelines and literature. Examinations were stored on the hard drive of the device and later on archived on Compact Disc Read-Only Memory (CD ROMs). Printouts of the results were archived in paper records; the results and measurements were transferred into the institute information system.

For descriptive statistic IBM SPSS Statistik 24 (IBM, Armonk, NY, United States) was used. Unless otherwise stated, the mean and standard deviation are given with the 95% confidence interval (95%-CI).

According to the regulations of the North Rhine Medical Association, Germany, the responsible authority for this study, a vote of the ethics committee was not necessary for this retrospective analysis.

Results

During the analyzed 14.5-year period, 6,110 PME with screening echocardiographies were included (5,923 were males and 187 females). Out of these, 4,477 applicants had a normal echocardiogram (4,349

were males and 128 females, age was 21.1 ± 3.3 [21.0–21.2] years, BMI was 23.3 ± 2.6 [23.2–23.4] kg/m²). The remaining 1,633 applicants (1,574 were males and 59 females, age was 21.1 ± 3.3 [95%–CI: 20.9–21.2] years, BMI was 23.2 ± 2.5 [95%CI: 23.1–23.3] kg/m²) revealed a total of 1,962 different abnormalities. Most common were tricuspid valve regurgitation (in 61.9% of the 1,633 cases), mitral valve regurgitation (20.0%) and ballooning mitral valve leaflet (7.5%). An overview of all findings is listed in Table 1.

Due to echocardiography findings, 77 applicants (1.26%) were assessed as unfit for flying duties, 9 (0.15%) were fit with limitations, and 1,544 (25.3%) were fit with findings that had to be monitored over time, but which were currently not aeromedically relevant. Tables 2, 3 list findings of applicants who were unfit for flying duties or fit with limitations, respectively.

Discussion

Out of 6,110 applicants within the analyzed 14.5-year period 1.26% were assessed as unfit, 0.15% were fit with limitations due to their echocardiographic findings. The most common diagnoses leading to disqualification or limitations were bicuspid aortic valve (BAV) with or without aortic regurgitation and/or dilatation of the ascending aorta (84.9, 1.2% of all applicants) and mitral valve prolapse (MVP) with or without regurgitation (9.3, 0.13% of all applicants). Although the number of abnormalities leading to disqualification or limitations was small, detection is important in the light of the challenging working environment of military pilots and a whole career of mostly several decades lying ahead of them.

In other studies, in this field, the rate of aeromedically relevant echocardiographic findings has been reported similar with up to 3.31% in the scientific literature (8, 9, 11). Depending on national aeromedical policies the disqualification rate could be lower (8, 9). So, an analysis of echocardiographic screening examinations by the United States Air Force School of Aerospace Medicine with 20,208 pilot applicants included shows a similar percentage of diagnoses (9). The disqualification rate, however, was much lower in that study especially for BAV, leading to the conclusion that screening echocardiography for military pilot applicants was deemed not efficacious.

Another retrospective study of 2,657 Israeli Air Force candidates found echocardiographical findings affecting aeromedical decisions in 3.31% of all candidates (8). They resulted in disqualification of 0.94% of all candidates, limitation to low-performance aircrafts in 0.83%, and need for follow-up in additional 1.54%. Another Israeli study analyzed 7,042 routine echocardiographies in air force academy applicants (11) specifically for BAV. BAV was found in 1.35% of those applicants, in 36% BAV was associated with mostly mild aortic regurgitation.

Echocardiography screening is also discussed in competitive athletes to exclude cardiac disease with an increased risk of sudden cardiac death (SCD) including cardiomyopathies (12–18). The authors of a survey across European Society of Cardiology member countries, however, conclude that in the absence of scientific evidence, before such practice is recommended, large studies using echocardiography in the pre-participation evaluation setting are necessary (19).

A major finding in our study and also in the analysis of Grossman et al. (11) was the number of BAV. This is similar to other prevalence

TABLE 1 Echocardiographic abnormalities.

Finding	<i>n</i>	%
Tricuspid regurgitation	1,029	61.9
Mitral regurgitation	332	20.0
Ballooning mitral leaflet	124	7.5
Pulmonary regurgitation	120	7.2
Aortic regurgitation	88	5.3
Bicuspid aortic valve	73	4.4
Hypermobile interatrial septum	36	2.2
Left ventricular enlargement	24	1.4
Patent foramen ovale	21	1.3
Interatrial septal aneurysm	20	1.2
Chiari network	13	0.8
Mitral valve prolapse	13	0.8
Hyperkinetic heart	11	0.7
Myxomatous mitral valve	11	0.7
Left ventricular hypertrophy	8	0.5
Left atrial enlargement	7	0.4
Diastolic dysfunction	5	0.3
Ectasia of the ascending aorta	5	0.3
Elevated pulmonary artery pressure	4	0.2
Hypermobile chorda of the mitral valve	4	0.2
Right ventricular enlargement	4	0.2
Atrial septal defect	1	0.1
Asynchronous left ventricular function	1	0.1
Reduced left ventricular ejection fraction	1	0.1
Reduced right ventricular ejection fraction	1	0.1
Annuloaortic ectasia	1	0.1
Interatrial thrombus	1	0.1
Aortic valve sclerosis	1	0.1
Right atrial enlargement	1	0.1
Ventricular septal defect	1	0.1
Status after cardiac surgery	1	0.1

One person could have more than one finding.

studies in the normal population, in which the prevalence of BAV is 0.5 to 2% in the United States (20). The valvular pathology commonly seen in BAV includes aortic valve stenosis, regurgitation, and infective endocarditis. The findings by Grossman et al. revealed that the cardiac morphology of young healthy individuals with BAV was affected irrespective of the presence or absence of mild or moderate aortic regurgitation. It was therefore recommended that aeromedical decisions should be based on the finding of BAV, and not on the presence of an associated aortic regurgitation (11). Because BAV confers an estimated 50% lifetime risk of requiring valve replacement and the procedures required for BAV management account for more morbidity and mortality than all other congenital heart diseases combined (20), it leads to disqualification for high-hazard occupations including flying a military aircraft in accordance with common

TABLE 2 Echocardiographic abnormalities in applicants who were unfit for flying duties.

Finding	<i>n</i>	%
Bicuspid aortic valve	56	70.0
Bicuspid aortic valve plus aortic regurgitation	15	18.8
Aortic regurgitation	2	2.5
Ectasia of the ascending aorta	1	1.3
Mitral and pulmonary regurgitation	1	1.3
Bicuspid aortic valve plus aortic regurgitation and mitral valve prolapse	1	1.3
Bicuspid aortic valve plus aortic regurgitation and ectasia of the ascending aorta	1	1.3

TABLE 3 Echocardiographic abnormalities of applicants who were fit for flying duties with limitations.

Finding	<i>n</i>	%
Mitral valve prolapse	7	77.8
Atrial septal defect	1	11.1
Pulmonary regurgitation	1	11.1

regulations (21, 22). In the USAF, BAV is also disqualifying, but a waiver can be granted for uncomplicated BAV.

In the German Armed Forces, applicants with BAV are usually unfit for flying duties, and also unfit for military service according to the German regulations (21, 23). The acceptable means of compliance issued by the European Union Aviation Safety Agency allows for fit assessment of professional pilot (class 1) applicants with BAV after referral to the licensing authority as long as no other cardiac or aortic abnormality is demonstrated (24). One reason why the military regulations in Germany are more stringent than the European civilian regulations is the exacting working environment of military pilots, especially for those flying high-performance aircraft, including acceleration, hypobaric hypoxia, tactical flying maneuvers, missions in austere environments, and possible enemy action (9). Another reason is the fact that in case of an employment, military pilot careers usually last for two to four decades during which an aggravation of the disease by their profession should be avoided. Overall, most individuals with BAV will develop valvular and/or aortic complications related to their BAV (20). As the fitness decision not only for military pilots but for military personnel at large is a long-term decision affecting the whole military career, the risk of employing those individuals is deemed too high by many armed forces, including the German Armed Forces.

The prevalence of mitral valve prolapse (MVP) is 1.3 to 3% in the general population (25). MVP alone is not necessarily disqualifying in the German Armed Forces but may lead to an exclusion from high-performance flying. Those associated with relevant mitral regurgitation, arrhythmia, bileaflet prolapse, thickened mitral leaflets, or mitral annulus disjunction are usually assessed as unfit for flying duties. Overall, MVP is a benign disease in most cases, associated with non-specific symptoms, such as atypical chest pain, exertional dyspnea, palpitations, anxiety, mid-systolic click, low blood pressure, and leaner build, which have come to be known as MVP syndrome. MVP can also be associated with electrocardiographic abnormalities and complex ventricular arrhythmias with polymorphic/right bundle branch block

morphology. The complications associated with valve disease include mitral regurgitation and less common infective endocarditis and cerebrovascular ischemic events. A subset of patients can experience cardiac arrest or SCD due to complex ventricular arrhythmias, which is a dramatic event that can affect these otherwise young healthy subjects (26). The incidence of SCD is estimated to be 0.14–1.8% per year in patients with MVP (27) with a prevalence of 2.3% (28), but it was reported to be as high as 7% in a young SCD population (13% in the female population) (29). The estimated rate of SCD in the general population is 0.06–0.08%/year, but the risk of SCD in MVP and cardiac patients is 1.73–2.3 times higher.

Screening echocardiography regularly reveals abnormal findings in young apparently healthy people. The most common ones are BAV with a prevalence of 0.5 to 2% (20) and MVP with a prevalence of 1.2 to 3% (25). Mild or moderate regurgitations of heart valves without morphologic changes are also common. The consequences of those findings, however, are a policy decision by the employer. If the prognosis and the likelihood of complications during a whole career is considered, the findings may more often lead to disqualification than if a fitness decision only relies on the current condition. The question if routine echocardiography for young and apparently healthy individuals should be implemented in applicant screening depends on such considerations for decision making. This is not only valid for pilots or non-pilot aircrew, but also for other high-hazard occupations including divers, astronauts, law-enforcement personnel, paramedics, off-shore workers, or professional drivers.

Aiming at harmonization or even standardization of air force screening programmes for pilot applicants, not only the prevalence of certain findings is important, but also the effect of certain findings on aeromedical decisions. While our study for example revealed that the percentage of BAV was similar to that in the US and other countries, the consequences are different, as in Germany BAV is not compatible with flying, while at least an uncomplicated BAV (without relevant regurgitation, stenosis, or infection) can be waived in the US. Therefore, a screening without echocardiography can more easily be justified in the US than in Germany, although a small risk of missing a BAV with aortic valve disease or other relevant findings has to be accepted.

Such retrospective prevalence studies in the specific age group of military pilot applicants is an important first step towards the harmonization of screening policies among allied countries and the improvement of international military cooperation. Perhaps aeromedical regulations and waiver guides will also have to be aligned over time. The results obtained in our study and in the whole project can also be applied to other high-hazard occupations. The recently

initiated three-year effort of the NATO working group HFM-386 will further elaborate these potentials.

Our study has some strengths and limitations, which have to be considered. One strength is that we could include all examinations for pilot applicants over the 14.5-year-period, because there is only one aeromedical examination center for the German Armed Forces, and because the German Air Force Centre of Aerospace Medicine used a digital documentation system. On the other hand, echocardiographies were performed by many different physicians during that timeframe. Therefore, a certain interobserver variability cannot be excluded. In addition, policies for aeromedical assessment might have slightly changed during that period of time as well as guidelines and recommendations for echocardiography in general. To reduce the effect of such changes, every examination was reevaluated regarding aeromedical fitness during our analysis.

It should also be recognized, that applicants for military aircrew duty receive a first screening in an assessment center based on medical history and a standardized questionnaire, before a profound aeromedical screening including echocardiography is performed. Thus, applicants with known heart disease are already classified as unfit during their basic screening. This means that the study population had been classified as a healthy population without any known (heart) disease as a result of their basic screening in the assessment center. The findings reported in our study have to be discussed against this background. Because our findings are similar to those of other studies (8, 9, 11), we think the bias caused by this effect is small for our cohort.

It should also be recognized, that the number of women examined here was low with only 3.1%. This was caused by a low overall proportion of women in the German Armed Forces of approximately 10%. An equal proportion of men and women could therefore not be expected in this cohort study, especially not in the group of pilots, where the percentage of women is much lower than in the whole German Armed Forces.

In summary, the percentage of abnormal findings in our study was similar to other studies and to that reported in the literature. Aeromedical assessments based on those findings, however, were slightly different and depend on national employment policies. As a consequence, the usefulness of echocardiography may vary between countries and different professions, depending on the acceptance of certain findings for employment. This and other studies aim at a harmonization of screening policies for pilot applicants and other high-risk occupations.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: analyzed datasets are property of the German Armed Forces (Bundeswehr). They are available upon reasonable request.

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Requests to access these datasets should be directed to Norbert Guettler, norbertguettler@bundeswehr.org.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

NG: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. SS: Conceptualization, Formal analysis, Investigation, Methodology, Software, Writing – review & editing, Writing – original draft.

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Conflict of interest

NG and SS are active Bundeswehr officers and work for the German Federal Ministry of Defence.

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The authors declare that no Gen AI was used in the creation of this manuscript.

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Assessment policy of post-traumatic stress disorder in aviation and its practical application using turbulence-triggered trauma as an example

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The U.S. Federal Aviation Administration (FAA) recently provided detailed instructions on how Aviation Medical Examiners (AMEs) should assess and evaluate pilots for post-traumatic stress disorder (PTSD). The European, Australian and International Civil Aviation Organization guidelines for the assessment of PTSD in aviation are general guidelines and do not address the unique and specific circumstances of a flight crew *per se*. The starting point of the U.S. FAA's guidance is an already-established clinical PTSD diagnosis since it is known that PTSD compromises aviation safety and has been related to fatal aviation accidents. According to the FAA's guidance, a PTSD assessment is undertaken based on whether the condition is symptomatic and medicated, or whether more than 2 years have elapsed since showing symptoms and receiving medication. The International Classification of Diseases (ICD) criteria for stress disorders have changed between versions ICD-10 and the soon-to-be-released ICD-11. The new ICD-11 criteria are discussed in this article in the context of aviation health. Additionally, PTSD, potentially caused by an incident of turbulence, is discussed in the context of aviation mental health. There are currently no published studies on turbulence-caused mental trauma. We have identified in this article potential factors which are related to pilots' and cabin crew's stressors in incidents of severe and extreme turbulence. Three recommendations are provided: (1) harmonize assessment practices of PTSD internationally; (2) healthcare professionals taking care of traumatized flight crew should have a follow-up guide that takes specific and local conditions into account, and ensures the identification of patients who require follow-up treatment as early as possible; and (3) aviation health care professionals should consider ICD-11 diagnostic criteria as the information may be more useful in the assessment and diagnosis of aviation-related trauma.

KEYWORDS

aviation, cabin crew, pilot, mental health, post-traumatic stress disorder, turbulence, International Classification of Diseases, Federal Aviation Administrator

Introduction

There is a well-recognized risk among aviation personnel, particularly pilots, cabin crew and air traffic controllers, of being exposed to traumatizing incidents related to flying. Practical and emotional support following traumatic events have been implemented at a practical level although debriefings are rare as this may impede speedy psychological recovery (1). According to the UK Civil Aviation Authority, individuals exposed to critical incidents should be immediately withdrawn from duty (2). Those individuals need time to rest, be available for medical examination if needed, have time to complete the necessary reports and be available to assist the investigating team. What constitutes a “critical incident” and determining its impact and severity on an individual will need to be clinically determined in each case.

Longer-term mental health effects caused by trauma are well known. However, there is a lack of longer-term follow-up studies showing the risk of developing post-traumatic stress disorder (PTSD) and related mental health conditions and symptoms following the specific context of aviation incidents and accidents, which by definition may impact a much wider number of people. A 1995 study of 6 cabin crew members in a turbulence-related aircraft accident in which 47 passengers were killed (3) reviewed cabin crew mental health interviews carried out between 8- and 10-months post incident. The study reported that all cabin crew members met the Diagnostic and Statistical Manual of Mental Disorders Third Edition Revised (DSM-III-R) diagnostic criteria for PTSD (the prevailing mental health classification system at the time) (4). All crew members subsequently developed a fear of flying, and they all also reported a fear of turbulence. The most intense and severe symptoms were reported by the most senior members of the cabin crew who had also suffered physical injury.

In 2009, an aircraft crashed near Amsterdam (5). Most adult survivors of the accident (passengers and crew) were followed up using the Trauma Screening Questionnaire at 2 and 9 months after the accident (6). A questionnaire was administered to 121 survivors including crew members and passengers. This study found at 2 months 46% and at 9 months 47% of participants were at risk of PTSD. At 2 months post-accident, there were 39 non-responders and at 9 months 45 non-responders in this follow-up study representing a significant rate of subject withdrawal from the study.

PTSD has been shown to be a risk factor for aviation safety (7). In this article, we discuss the assessment policy after exposure to trauma in aviation. Of particular interest is the U.S. Federal Aviation Administration's (FAA's) protocol that was introduced in June 2024 for assessing PTSD in pilots (8). In the article herein, we consider the applicability of this new FAA protocol in assessing the fitness to work/operate aircraft by aircrew experiencing stress-related symptoms after significant turbulence.

The purpose of this Policy and Practice Review is to raise awareness of the updated diagnostic criteria for PTSD that differs between the ICD-10 (International Classification of Diseases diagnostic system) and the new ICD-11 system. Additionally, PTSD aviation medicine assessment protocols provided by different aviation authorities are compared. Furthermore, the potential role of turbulence as a trigger for PTSD is discussed. We also consider why

there is a need to follow-up with flight crew after such incidents. To the best of the authors knowledge there are no published studies on this topic in aviation medicine.

Methods

Literature searches were carried out in August 2024 via the Medline and Cochrane databases to identify relevant research articles, reviews, or systematic reviews focusing on PTSD, ICD-10, ICD-11, and fatal Aviation Accidents. The medical requirements of different aviation authorities from the U.S. FAA, Australia (Civil Aviation Safety Authority), Europe (European Aviation Safety Agency), and the International Civil Aviation Organization (ICAO) Manual of Civil Aviation Medicine were examined and compared using information from the websites of these organizations. The data relating to recent turbulence accidents were based on accident reports and relevant newspaper articles.

Trauma-related stress disorder in the International Classification of Diseases diagnostic system

The Diagnostic and Statistical Manual of Mental Disorders (DSM), published by the American Psychiatric Association (APA), is used in the U.S. and in other jurisdictions to diagnose and classify psychiatric symptoms and conditions (9). The International Classification of Diseases (ICD), produced by the World Health Organization (WHO), is used in Europe (10). The current versions in use are DSM-5 and ICD-10, respectively, which are revised and updated periodically. DSM and ICD systems diagnostic criteria differ in some aspects (Table 1). For example, in the forthcoming update from ICD-10 to ICD-11, there is a narrower concept for PTSD, and both acute stress reaction and acute stress disorder will no longer be diagnostic entities while they are still present in the older ICD-10 and DSM-5 (10, 11). The appropriateness of the ICD-11 diagnostic criteria for stress related disorders in clinical practice has been studied to some extent by Ederle & Maercker (12). This study showed that stress-associated disorders, as defined by ICD-11, have discrete features typical for each diagnostic group. Furthermore, it was shown that in each diagnostic group, cognitive thinking styles, such as preoccupation, were associated with flashbacks and rumination. Additionally, Møller et al. (13) studied how well ICD-11 diagnoses of PTSD overlap with ICD-10 diagnoses. In their study of 165 Danish psychiatric outpatients they found that 23% with ICD-10 PTSD did not meet the ICD-criteria for a PTSD diagnosis. This finding is supported by other studies (14, 15). The result is somewhat expected because ICD-11 diagnostic criteria focus on core post-traumatic responses and should potentially reduce overlap with depression and anxiety (13). The results are mainly based on psychiatric data obtained from psychiatric patients. It remains to be seen if this change in diagnostic criteria affects PTSD diagnosis in aviation medicine.

ICD-10 is used as the diagnostic basis for ASR (acute stress reaction), ASD (acute stress disorder) and PTSD. Additionally, potential new challenges are discussed relating to new diagnostic criteria of stress disorders prescribed by the new ICD-11 in the context of flight personnel aeromedical assessment. Stress diagnoses defined

TABLE 1 Comparison of International Classification of Diseases (ICD) systems (10, 47).

Disorder	ICD-10	ICD-11
Acute stress reaction	Occurs within minutes of the triggering event and resolves rapidly if the stressor is removed, and within 1–3 days even if it is not.	No longer a diagnostic entity.
Acute stress disorder*	Symptoms begin within 4 weeks of the trauma and last a minimum of 3 days, but no more than 1 month.	No longer a diagnostic entity.
Posttraumatic stress disorder*	Experiencing threatening or catastrophic event Intrusive flashbacks Avoidance Changes in cognition and mood Either A or B: A. Inability to recall, either partially or completely, some important aspects of the period of exposure to the stressor. B. Persistent symptoms of increased psychological sensitivity and arousal All criteria must last several weeks and met within 6 months of the stressful event.	Experiencing an extreme threatening event Re-experiencing Avoidance Persistent perceptions of heightened current threat The symptoms must last for at least several weeks. Significant functional impairment.
Complex posttraumatic stress disorder	Not covered	Experiencing an extreme threatening event. Characterized by the core symptoms of PTSD as well as persistent impairments in affective, self- and relational functioning, difficulties in emotion regulation, beliefs of being worthless, difficulties in relationship.

*Are diagnostic terms in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (48).

in ICD-11 associated with prolonged stress such as prolonged grief disorder are also covered herein.

PTSD in the diagnostic and statistical manual of mental disorder diagnostic classification

It is noteworthy that DSM-5 has taken a broader approach to PTSD compared to that of ICD-11. In addition to core symptoms of PTSD intrusions, avoidance and arousal activity, DSM-5 includes symptoms related to mood changes such as negative beliefs, having distorted thoughts, negative emotions, reduced interest in significant events and feeling detached. [Supplementary Appendix 1](#) lists PTSD diagnostic criteria based on DSM-5.

Prolonged grief disorder

A new diagnostic disorder in ICD-11 associated with stress is prolonged grief disorder (10, 11). The diagnosis describes abnormally persistent grief. It is defined as a persistent and pervasive yearning for the deceased following the death of a person close to the bereaved, or a persistent preoccupation with the deceased. Symptoms extend at least 6 months and cause significant impairment in the person's functioning. With this disorder symptoms of grief go far beyond a person's cultural context. The evidence for this new diagnosis comes from a variety of cultures (16). In addition to grief, these patients have mental health problems associated with suicidality, substance abuse and harmful health behaviors and cognitive dysfunctions (16, 17). Prolonged grief disorder also has been introduced in DSM-5-TR, and there are some differences compared to ICD-11 diagnostic criteria (18). This disorder is discussed briefly herein because it is new and potentially related to flight crew health assessment.

Assessment protocol for PTSD by different aviation authorities

Assessment protocol for PTSD in Aviation by International Civil Aviation Organizations, Civil Aviation Safety Authority Australia and European Union Aviation Safety Agency

The European, Australian and International Civil Aviation Organization guidelines for the assessment of stress reactions in aviation are general guidelines and do not address the unique circumstances of flight crew *per se* (Table 2) (19–21). The assessment of PTSD has not been elevated to a special status in these guidelines, and the scope of the assessment remains largely discretionary.

Assessment protocol for PTSD in aviation by the U.S. FAA

The FAA recently provided detailed instructions on how Aviation Medical Examiners (AME) should assess and evaluate pilots for PTSD disorder. These very detailed instructions are unique among air medicine guidance. As mentioned above, it is typical for authorities to instruct an evaluation on a general level, whereas the starting point of the FAA's guidelines is an already-established PTSD diagnosis (8). In such cases, the evaluation is performed differently based on whether PTSD is symptomatic and medicated, or whether more than 2 years have elapsed since symptoms were identified and medication started. In the latter case, if there have been no symptoms or medication for 2 years, the AME can make an assessment independently (Table 3).

The FAA's guidelines place more weight on previous mental health symptoms. To evaluate these conditions, a pilot-completed questionnaire has been devised (Table 4) (22). If a positive answer is provided to any items on the questionnaire, decisions regarding fitness

TABLE 2 Guidance Provided by ICAO, CASA Australia and EASA of the Assessment Stress Related Disorders (19–21).

Authority/ Organization	Guidance
ICAO	Psychiatric symptoms due to external stressors leads to being temporarily unfit. Reassessment after a period of stability without use of psychotropic medication. Note alcohol and/or other psychoactive substances use.
CASA Australia	General assessment for all psychiatric disorders: Symptoms, medications, recurrence, risk of harm to self and others and comorbidities and organic causes.
EASA	Signs or evidence that applicant has stress-related disorder, then needed psychologic or psychiatric opinion and advice

to fly are immediately transferred to the crew licensing authority for further evaluation.

Practical examples of aircraft accidents and stress/PTSD

Trauma follows from an event that poses a significant challenge to the emotional and/or physical safety of person involved in the situation, whether directly or indirectly exposed to the triggering situation or event (23). Regarding aviation, a traumatic experience comprises in-flight events and as well as events related to the rescue operation. It has been shown in studies in which victims of aviation-triggered PTSD were followed up, the risk factors related to this disorder were loss of relative in the aircraft accident, the severity of physical symptoms and the severity of the event itself (24).

In an accident involving SK751 flight on 27 December 1991 from Stockholm to Warsaw 129 persons onboard who all survived, the aircraft MacDonnell Douglas MD-80 rapidly descended due to a loss of engine power and some minutes later crashed onto a field. An opportunistic, follow-up study of PTSD among those people on board was carried out (25). There were initially high levels of PTSD. Most changes in the presence of PTSD symptoms occurred between 1 and 4 months and after that there was only a small decrease occurred from 4 to 25 months.

Turbulence related incident and stress

In-flight turbulence may be a specific trigger trauma and PTSD. In the recent analysis medical data, which compared turbulence events between 2019 and 2023, it was shown that there was an increase in turbulence-related injuries over this period and that about 10% of these incidents caused acute stress reactions (26). The analysis involved specifically business aviation and found that that in 2019, 123 cases of injury and in 2023, 187 cases of injury attributed to turbulences. Among these cases, there were 47 and 53 crew members in 2019 and 2023, respectively, injured due to turbulence. These incidents can trigger PTSD in those injured in such circumstances.

The recent incident from commercial aviation will be introduced. On the 21st of May 2024 Singapore Airlines flight SQ321, carrying 211 passengers and 18 crew members, was involved in a serious turbulence

TABLE 3 FAA U.S. assessment protocol for PTSD (8).

	AME	FAA
Condition	No PTSD symptoms and no SSRI* or other psychiatric medications in the past 2 years	PTSD symptoms and/or SSRI or other psychiatric medications
Evaluation	Information regarding 1) diagnosis 2) severity 3) treatment 4) symptoms 5) fill in <i>Anxiety, Depression, and Related Condition Tool for the AME</i>	<i>Airman statement covering</i> 1) incident(s) 2) triggers and symptoms 3) impact for life 4) modifications to work 5) medications 6) any form of counseling <i>Current evaluation psychiatrists/ psychology</i> <i>Medication list</i> <i>Copies of PTSD screening tools</i>
Assessment	AME may assess	FAA will assess

*SSRI, selective serotonin reuptake inhibitors.

TABLE 4 Anxiety, depression, and related conditions decision tool for the AME (22).

Questions to be considered
Any other mental disorder diagnosis or symptoms?
History of suicide or self-harm?
History of involuntary mental health condition or substance use?
History of electroconvulsive, transcranial magnetic, ketamine, or psychedelic therapy?
History of psychiatric hospitalization?
Individual experienced more than one episode?
Continued symptoms severe enough to interfere with safety?
Mental health medications?
Is AME having any concerns?

incident that resulted in 70 injuries and one death (27). The initial report by the National Transportation Safety Board of Singapore mentioned that the first vertical acceleration decreased from +1.35 G to −1.5G resulting in those cabin crew and passengers who were not wearing seat belts becoming airborne. Vertical acceleration then changed from −1.5 G to +1.5 G resulting in those same passengers and crew falling back down, resulting in severe injuries (28).

The paucity of studies is noted about the mental symptoms of pilots and cabin crew after highly stressful events caused by turbulence that negatively affect both their physical and psychological health. In addition to symptoms related to short term acute stress reactions, mental and physical traumas related to serious incidents like turbulence, may potentially be associated with an increased risk of developing PTSD (29, 30). Our current understanding of the PTSD risk in flight crew is based on limited studies of aircraft crash accidents (3, 5).

A National Transportation Safety Board (NTSB) analysis of commercial aircraft operations from 2009 through 2018 found that

turbulence-related accidents were among the most common types of accidents accounting for one-third of incidents and accidents recorded and their number is increasing (31–34). According to ICAO's 2024 Annual Safety Report, turbulence-related accidents were around 40% of all accidents involving large aircraft (34). In addition, most turbulence-caused accidents resulted in one or more serious injuries (33). The NTSB report offers flight-safety-related technical operational recommendations as well as new recommendations for cabin crew pertaining to the phases of flight and altitude at which cabin crew should be secured in their seats. Additionally, the report recommends improving in-flight communication between pilots and cabin crew.

Most of the turbulence-related incidents reported to the NTSB were moderate or severe. During moderate turbulence, passengers may feel strain against seat belts while during severe turbulence passengers are violently forced against their seat belts (assuming that they are “strapped in”). During extreme turbulence, the aircraft may be impossible to control, passengers may suffer severe injuries, and the aircraft may undergo structural damage. In the above-mentioned NTSB report, there were 97 seriously injured cabin crew members, and over 80% of them were not using seat belts when turbulence occurred (33). Most serious injuries were related to the lower and upper extremities and spine.

While there are no studies currently available on turbulence-caused mental trauma, there are potential stressors that could be key predictors in identifying air crew mental health issues due to being exposed to severe turbulences (Table 5). The type and strength of stressors are different among cabin crew and pilots and depends on the incident type. Furthermore, immediate post-incident stress could be exacerbated by reports and incident investigation, which in turn may impact upon pilots and cabin crew differently.

From the aviation medicine assessment perspective, there is the need for acute support, followed by assessments relating to when pilots and cabin crew are fit to return to duty. This should be followed by timely follow-up with longer-term assessments completed due to the risk of developing PTSD. The U.S. FAA recommends that PTSD assessment should be performed earlier when dealing with significant mental health history as it can be an important risk factor for PTSD (8). A recent systematic review of road accidents found that female sex, sociodemographic markers, pre-trauma, peri-trauma, and post-trauma factors were predictors of PTSD (35). PTSD was assessed

between 2 weeks to 3 years post-incident. The significant predictors of PTSD were being female, pre-existing depression, previous road traffic accidents, peritraumatic dissociative experiences, acute stress disorder diagnosis, rumination, injury severity, and involvement in litigation after trauma. While these results are derived from studies of road accidents, they could be applicable to risk-profile assessments of pilots and cabin crew following turbulence-related incidents. In this situation, it is not enough for aviation occupational health care specialists to identify the immediate factors related to the trauma itself (although they also need to be carefully identified); it is important to understand the diverse risk factors underlying the risk of PTSD.

Traumatic incident in the aviation occupational healthcare

When using the ICD-10 diagnostic criteria, PTSD diagnosis is usually performed after approximately 6 months but can be performed as early as 1 month. A common challenge, based on clinical experience, is that it is not easy to keep the crew under close supervision after an incident. To be able to assess the occurrence and development of possible symptoms experienced by the crew, it would be helpful if a structured interview related to the symptoms of trauma was conducted for every member of the crew exposed to a significant stressor. These structured interview templates would be available to suit different diagnostic systems (36–38). There is no uniform practice regarding the timing of assessments and structured interviews after aviation accidents. However, it is important especially regarding the flight crew that they cover the early stages, and that follow-up includes a patient appointment before returning to duty. Based on the results of the first assessment and the structured interview it is important to schedule the follow-up assessments including the interviews. The second assessment and interview are recommended to be scheduled within 3 months because trauma symptoms during recovery from PTSD following acute trauma exposure according to systematic review occur mainly during the first 3 months after trauma (39). The follow-up needs to be more in depth and longer lasting for crew members with an increased risk of PTSD as well as with those that are symptomatic. Table 6 presents the practical functions of aviation occupational health care in the treatment of aviation mental trauma. Especially continuous education is utmost important since the EASA MESAFE Report has shown that some AMEs may have insufficient experience regarding psychological and psychiatric assessments (30). This survey revealed that almost half of the respondents do not have consistent and effective criteria to decide whether to refer a pilot to a mental health specialist.

Discussion

There is limited evidence that PTSD presents itself in some fatal aviation accidents (3, 7). We found in the NTSB accident database between 2000 and 2015 eight pilots with a diagnosis of PTSD, two of whom had aviation-related PTSD. Also, the lack of follow-up studies after traumatizing incidents was noted. Additionally, these studies showed that pilots did not inform their AME or employer of their pre-existing mental symptoms. Currently, there is a lack of research on PTSD as a risk factor for aviation accidents (40). There is a culture

TABLE 5 Potential turbulence incident related acute stressors among pilots and cabin crew.

Turbulence type	Pilots' stressors	Cabin crew's stressors
Severe	Aircraft control Application of protocols and sufficiency of crew-resource Acute situation in cabin	Own injuries Behavior of colleagues and their injuries Passengers' behavior and their injuries
Extreme	Own injuries Aircraft control due to damage and sufficiency of crew-resource management Flight protocols not applicable Acute emergency in cabin	Own injuries Behavior of colleagues/pilots and their severe injuries and possible deaths Passengers' behavior and their severe injuries and deaths

TABLE 6 Practical functions of aviation occupational health care in the treatment of aviation mental trauma.

Function	Practical action
The role of airline providing acute psychological support	Advance preparation and agreement on consultation readiness with clinical/aviation psychologists and psychiatrists
Long-term support	Systematic monitoring of trauma symptoms through structured interviews, especially during the first 4 months after accident
Continuous education	Identification and treatment of trauma symptoms associated with aviation accidents using appropriate consultations
Accidents/incidents	Because accidents/incidents may happen anywhere in the world, the airline must create an international cooperation plan.
Periodical medical examinations*	Ask whether the person being examined has been exposed to accidents/incidents

*Periodical medical examinations are carried out for airline pilots at least once a year but for cabin crew, varying depending on the country. In Europe examination is carried out for cabin crew at least every 5 years but f. ex. in the U.S. only when starting work.

within aviation that not to report mental health related symptoms to AME because of fear losing career and medical certification. There is also existing a distrust in the aviation authority medical assessment and much of this distrust is due to lack of information about the aviation authority processes (41).

Aviation health regulators have until recently dealt sparingly with pilot PTSD assessment, and the new U.S. FAA protocol is welcomed. Considering the concern highlighted herein, there is an urgent need to address PTSD further and on an international basis. Whether there is a need for detailed PTSD-specific assessment protocols or more formal adoption of more frequent cycles of general mental assessment (to include mental health risk analysis) with PTSD needs to be discussed. There is a great need to increase awareness of PTSD as a potential disorder affecting flight safety. With the frequency of serious turbulence incidents predicted to rise, in line with climate change, it is reasonable to conclude that the rates of mental trauma experienced by air crew because of these changes in climatic conditions are going to increase (42). The evaluation of cabin crew has not been required until now, and the protocols for doing so are not clearly articulated. The current situation requires more detailed instructions for the cabin crew. PTSD diagnostic criteria are changing, and the ICD-11 system will be introduced in the near term. Aviation occupational health units need to take account of this change in their training. It is also worth considering that as part of ICD-11 there are new diagnoses such as prolonged grief disorder and complex PTSD.

There is a growing literature using new methodologies to study PTSD. For example, there are studies using functional MRI and neural network modeling to research subtypes of PTSD (43, 44). It is possible that these new results will offer improvement in diagnostics as well as new and specific options for the treatment of PTSD. Better diagnostics (40) and new therapeutic methods (45) should allow even more air personnel to return to work after severe traumatic events. In neural contributors to trauma resilience, neuroimaging studies have shown individual differences in neural

function that appear protective against the psychopathology following a major life stressor (46).

As already mentioned, there is a specific lack of studies about the mental symptoms of pilots and cabin crew after highly stressful events caused by turbulence, or indeed related traumatic ground- or in-flight untoward and potentially traumatic events. In this review, we have identified potential factors that are related to pilots' and cabin crew's stressors in incidents of severe and extreme turbulence and potentially are triggers of PTSD. Medical and psychological follow-ups of aircrew several months after severe turbulence are necessary to identify those pilots and cabin crew members who manifest PTSD. PTSD is harmful to an individual, but it also may compromise flight safety. Returning to flight duty after PTSD needs careful assessment. The assessment protocol provided by the U.S. FAA is a welcomed addition, but it is recent, and there is still little experience in its practical application. Even though data are scant, it is well-accepted that trauma can trigger PTSD. The intention of this article is to raise awareness to motivate aircraft pilots and crews, investigators, healthcare practitioners, and researchers to consider turbulence as another potential trigger in their assessments, gather more data and continue to develop policies and protocols to improve aviation safety.

Findings

- 1) Aviation personnel are at increased risk of being exposed to traumatizing incidents associated with ground operations and actual flight.
- 2) Aviation personnel risk developing PTSD which compromises personal well-being and potentially flight safety. It also may lead to attrition in aircrew.
- 3) The diagnostic criteria for PTSD are currently changing because of modifications from ICD-10 to ICD-11.
- 4) Different aviation authorities have differing medical assessment protocols for pilots diagnosed with PTSD.
- 5) Turbulence-related incidents appear to be increasing in frequency.
- 6) Severe turbulence may be a trigger for PTSD although there is a lack of research studies to support this position.
- 7) There is a need to follow-up aviation personnel after severe turbulence and to create a protocol for this purpose.

Recommendations

- 1 The U.S. FAA has recently prepared in detail an assessment protocol for PTSD.

Harmonize international assessment practices of PTSD in aviation medicine so that aviation authorities throughout the world can prepare assessment protocols for PTSD that are based on upon consistent criteria. A similar type of protocol can best ensure that the assessment and monitoring of flight crew performance are carried out routinely, effectively and with adequate comparison. This protocol should also include a recommendation on international cooperation in acute situations.

- 2 Follow-up guidance should be issued for healthcare professionals who take care of traumatized flight crew that also takes local conditions into account, which ensures the identification of patients who require follow-up treatment as early as possible.
- 3 Healthcare providers should move from ICD-10 diagnostic criteria to those in the ICD-11 diagnostic criteria. There are differences between the criteria in each document regarding acute and long-term diagnostic criteria. Aviation occupational healthcare units need to update their knowledge and understanding of these changes. In this regard, AMEs have a requirement for continuous training; these training sessions should cover the identification and monitoring of PTSD and assessments in terms of airworthiness.

Limitations and practical applications

The major limitation in this review is that there is a lack of published literature on aircraft turbulence-related incidents and the association with PTSD. Additionally, there is very little research on PTSD related to aircraft incidents and crashes. This dearth of data makes it challenging to estimate the prevalence of PTSD associated with aviation accidents. Regardless, as a practical application we have highlighted the need to follow-up aviation personnel after severe turbulence. This review does not cover the mental trauma that has occurred to passengers onboard and their loved ones, ground personnel, air traffic controllers, rescue personnel and forensic personnel.

Author contributions

AV: Writing – original draft, Writing – review & editing. RB: Writing – original draft, Writing – review & editing. BB: Writing – review & editing. AG: Writing – review & editing. A-SS-M: Writing – review & editing.

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Supplementary material

The Supplementary material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpubh.2025.1505004/full#supplementary-material>

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Peripheral skin cooling during gravitational challenges in parabolic flight – experimental protocol, implementation, and case study of the CoolFly experiment

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Objective: Ensuring cardiovascular stability is critical for the lasting and prosperous success of human spaceflight. Astronauts are exposed to dynamic acceleration profiles and prolonged changes of gravity which pose serious acute and long-term health risks. Parabolic flight is a model for gravity induced cardiovascular instability. In this proof-of-concept, we aim at analyzing the feasibility and effectiveness of peripheral cooling (PC) as a countermeasure during parabolic.

Methods: In this study, we employed a cross-over trial to investigate the effectiveness of PC in enhancing cardiovascular tolerance during gravitational changes simulated via parabolic flight. Continuous, non-invasive blood pressure, heart rate, peripheral oxygenation and brain oxygenation, peripheral blood flow, as well as skin and brain temperature were assessed. This study is a proof-of-concept for experimental feasibility and qualitative effectiveness of PC during parabolic flight.

Results: Our case study data showed reductions in heart rate of 10.0% (6.79 bpm) and reduced changes in heart rate during gravitational changes (standard deviation 12.55 vs. 10.37 bpm). Further, we observed reduced blood pressure reactions to altered gravity (−20/+39 mmHg vs. −9/+8 mmHg), with minimal changes in skin (0.27°C) and brain core temperature (0.14°C) as well as reduced changes in micro-perfusion comparing PC with control.

Conclusion: This proof-of-concept study demonstrates that peripheral cooling is feasible during parabolic flight and may attenuate cardiovascular responses, as indicated by reduced heart rate and blood pressure

fluctuations. These preliminary findings support further controlled studies to assess PC as a non-invasive countermeasure to changes in gravitation.

KEYWORDS

space, orthostatic in, cardiovascular stability, blood pressure, extreme environment, countermeasure

Introduction

Human life has evolved under Earth's gravitational conditions. In consequence, human physiology is adapted to this environment, ensuring a constant and sufficiently oxygenated blood flow to all vital organ systems (Silver and Siperko, 2003). The gravitational force markedly determines fluid distribution within the body. This is particularly evident in instances of postural change, which can lead to alterations in cardiac pre- and after-load, and in the clinical manifestations of orthostatic hypertension (Klijn et al., 2015; Ricci et al., 2015).

Similar effects have been observed during human spaceflight. These include a marked caudal to cranial fluid shift when in microgravity and a prominent inverse redistribution after returning to planetary gravity (Hargens and Watenpaugh, 1996; Demontis et al., 2017). In response, the cardiovascular system detects an increased pre-load and actively downregulates cardiac chronotropy, inotropy, vascular resistance and blood volume to limit blood flow and pressure to the vital organs and prevent damage under the condition of microgravity (Tanaka et al., 2017; Gerber et al., 2018). Adaptation to these conditions leads to a severe cardiovascular deconditioning, represented by a decline in baroreceptor responsiveness, reduced cardiac reserve, relative hypovolemia and altered autoregulation. This culminates in post-flight orthostatic intolerance, experienced to various extents by all long-term space travellers (Blaber et al., 2011; Lee et al., 2015; Fu et al., 2019).

These changes are critical for the management of astronauts' health after return to Earth. Furthermore, the diminished performance observed in the post-landing phase, which may potentially lead to orthostatic intolerance, is likely to constitute a significant challenge for future crewed missions aimed beyond low-Earth orbit (BLEO) (Baker et al., 2019; Moore et al., 2019). To ensure astronaut's health, these new mission profiles demand safe, effective, and reliable countermeasures, that are not dependent on Earth-bound capabilities (Doarn et al., 2019; Scott et al., 2023). It is imperative that all countermeasures undergo a rigorous evaluation in spaceflight analogues prior to their implementation in space, such as parabolic flight.

Parabolic flight offers an excellent combination of rapid gravitational changes (hyper-gravity = 1.8 g, normo-gravity = 1.0 g, micro-gravity = 0.0 g) which induces acute physiological reactions that can be measured in real-time (Ploutz-Snyder, 2016; Cromwell et al., 2021). The richer and more robust the data produced in these contexts, the greater our assurance in the effectiveness of the suggested countermeasures. However, physiological monitoring during parabolic flight is highly complicated. The extreme, changing environment and short-term duration of gravitational states during parabolic flight necessitate careful selection of measurement paradigms. In cardiovascular monitoring, electrical signals (such

as Electrocardiograms (ECG)) can be recorded comparably simply and reliably (Beckers et al., 2003; Verheyden et al., 2005). To the contrary, real-time measures of blood pressure (BP) are already highly complicated on the ground (Kario et al., 2024; Pilz et al., 2024). Multiple studies have provided data using finerpethysmographic devices during parabolic flight (Schlegel et al., 1998; Limper et al., 2014). While feasible if conducted carefully, this technology is highly prone to measurement artefacts such as induced by changes in posture (gravitational effect) and temperature changes (vascular effect) (Wesseling, 1996; Romano et al., 2002). New measurement technologies (e.g., based on the pulse-transit-time) have been shown to provide comparably reliable and easily recordable BP measurements, even under highly dynamic physiological conditions (Pilz et al., 2022; Kario et al., 2024). Lastly, the combination of Laser-Doppler Flowmetry and parabolic flight proven near-infrared-spectroscopy provides a comprehensive measurement approach to monitor peripheral blood flow and oxygenation (Schneider et al., 2013; Shepherd and Öberg, 2013). The application of peripheral cooling (PC) further necessitates the monitoring of changes in body temperature.

We hypothesized that peripheral cooling (PC) could be an effective countermeasure to orthostatic intolerance, based on the physical response to cooling in form of a cutaneous vasoconstriction, increasing the total peripheral resistance and thereby after-load and arterial blood pressure (Charkoudian, 2010; Khoshnevis et al., 2015; Alba et al., 2019; Seeley et al., 2021). This effect of cold exposure has been described extensively in laboratory conditions (Durand et al., 2004; Korhonen, 2006). Clinically this is most impressively highlighted by the fact that cold winter temperatures lead to population wide increases in blood pressure (Stergiou et al., 2020). Beyond that, the number and severity of incidents of orthostatic intolerance is greatly amplified during the summer months, as the increased temperatures induce a peripheral vasodilation with subsequent blood pressure drop (Narkiewicz and Somers, 1998; Stergiou et al., 2015). It further already has provided promising results in improving orthostatic intolerance after multi-day head-down tilt bed rest, another Earth-bound spaceflight analogue (Keller et al., 2011).

Combining low-heat-conducting carbon-gel cooling pads with the TRPM8 activator menthol in a topical gel is a promising approach as it induces a strong cold sensation (critical for the induction of vasoconstriction and therefore potentially cardiovascular stabilisation) without meaningfully lowering core body temperature (Lee et al., 2012; Voronova et al., 2022). More precisely, the menthol induced vasoconstriction can lead to an increase of body temperature, counteracting the small temperature effect of carbon-gel cooling pads (Gillis et al., 2010).

This study assesses the effectiveness of PC as a countermeasure to orthostatic challenges during changes in gravitational force. The results presented here are based on a proof-of-concept analysis

of the findings from the CoolFly experiment, which took place as part of the German Aerospace Agency's (DLR) 39th parabolic flight campaign.

Methods

Participants and experimental location

The CoolFly experiment was conducted during the DLR's 39th parabolic flight campaign, at Novespace in Merignac, France. A single subject ($N = 1$) has been included. The subject was a healthy, 34-year-old male with no prior micro- or hyper-gravity exposure. Exclusion criteria included any cardiac, pulmonary, neurological, or other system illness. Written informed consent was obtained from the subject before participation.

The experiment consisted of two parabolic flights, each conducted on a separate day. Each parabolic flight itself consists of 30 unique parabolas, flown in sets of five. After each parabola there is a period of steady flight of 1 minute. After each set of 5 parabolas, there is a 5-min break. After the first 3 sets of 5 parabolas each (halfway point), there is a longer pause of 8–12 min.

A parabola maneuver describes the plane pitching up from steady flight at full thrust to 47° for 20 s, creating 1.8 g (hyper-gravity) in the cabin. After the ascend, the thrust is set to minimum, allowing the plane to follow a parabolic trajectory, creating a micro-gravity (~ 0 g) environment in the plane for 22 s. In this process, the plane pitches down to 45° . To break the fall, the plane pulls up again for a period of 20 s, again creating an environment of 1.8 g.

To limit motion sickness during the parabolic flight, the subject was given an intra-muscular injection of Scopolamine by the medical team of Novespace on both flight days before boarding the airplane. Further, to mitigate the potential effects of scopolamine on the experimental results, the subject received a minimal intramuscular dose of 0.005 mg/kg Scopolamine 90 min before the onset of the parabolas. As cold temperatures aboard the plane could induce physiological reactions affecting our experimental outcome, Novespace agreed to conduct this parabolic flight at 23°C (unlike the typical 17°C – 20°C). Moreover, the participant wore a T-shirt during the control parabolas to protect him from potential wind-chill effects induced by the aircraft's air conditioning.

Experimental protocol

Experimental design

We evaluated the effectiveness of PC as a countermeasure to orthostatic stress during parabolic flight in a cross-over controlled case study design. To minimize the bias induced by the increased mental load during the first (excitement about first flight) and last set of five parabolas (getting ready for end of experiment), only data from the second until the fifth set of parabolas was analyzed for stress dependent parameters (e.g., heart rate). The subject was measured in a standing position during the full experiment and was advised to not use the muscle pump to actively counteract orthostatic effects. To homogenize the mental load and excitement state as much as possible, the subject was asked to perform psychometric tests

(Flanker Test) (Sanders and Lamers, 2002) on a tablet computer during the parabolas.

Peripheral cooling

To induce a cutaneous vasoconstriction and thereby increase total peripheral resistance, afterload and blood pressure, we applied a combined PC countermeasure. As vasoconstriction is dependent on the activation of cold-sensitive TRP-channels, sensing a cooling of the skin surface temperature, and not on core-body energy drainage, we opted for a combination of carbon-gel cooling pads (Aubdool et al., 2014; Pan et al., 2018). These were fixated by cooling garments (CarbonCool, Global Healthcare SG, Singapore) to the lower extremity and abdomen and back and the application of a long-lasting menthol gel (BioFreeze, Reckitt Group, United Kingdom) (Charkoudian, 2010; Voronova et al., 2022). The carbon-gel cooling pads remain cold for a prolonged period, leading for a steady-state PC during the whole flight. The menthol gel additionally induced a cold-sensation by activating temperature-sensitive TRP channels and without further cooling down the participants (Bautista et al., 2007). The cooling garments and menthol gel were applied and attached to the test subject during the flight, immediately before the commencement of second 15 parabolas.

Physiological measurement

Heart rate (Faros, SOMNOtouch NIBP, ABPMpro)

We recorded an electrocardiogram (ECG) in a full Holter configuration with three different devices. This was done to create redundancy and ensure maximum measurement quality for potential heart-rate variability analyses. The Faros 180 (Bittium, Finland) was used to record only the ECG. The Somnotouch NIBP and ABPMpro (both SOMNOMedics, Germany) devices were also used to record ECG data. The ABPMpro also offers preliminary impedance cardiography capabilities.

Blood pressure monitoring (SOMNOtouch NIBP, ABPMpro)

The two devices were also used to monitor the continuous and non-invasive blood pressure, relying on a pulse-wave-velocity measurement approach. The SOMNOtouch NIBP detects the pulse-arrival-time, derived from the ECG and a SpO_2 finger clip (Bilo et al., 2015; Socrates et al., 2021; Bothe et al., 2023). The ABPMpro measures the pulse-transit-time (pulse-arrival-time corrected for cardiac pre-ejection period) from an ECG and a photoplethysmography sensor placed at the upper arm (Pilz et al., 2023). The device also offers a validated oscillometric, cuff-based blood pressure measurement capability which was used to calibrate both devices' continuous measurement in between sets of parabolas to optimize measurement accuracy (Roth et al., 2023). For this, automated cuff-based blood pressure measurements were initiated with the device during steady flight. The cuff-based reference values were used to calibrate the continuous blood pressure estimation in a post-measurement analysis, as recommended by the device manufacturer. In addition, the ABPMpro detects changes in the gravitational force through its inbuilt accelerometer. Both devices

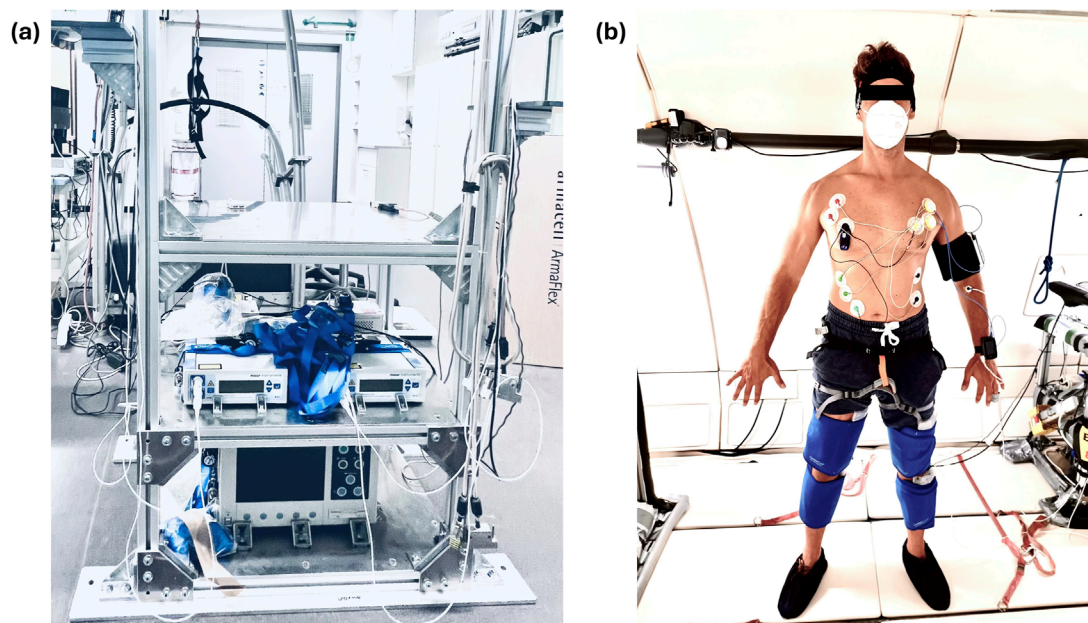


FIGURE 1

The left panel (a) shows the experimental rack. The data recording laptop was later attached to the top shelf computer, the Laser Doppler monitors (mid shelf) and the NIRO 200 near-infrared spectroscopy device (bottom shelf). The right panel (b) shows the measurement sensor placement displayed on a researcher who provided his consent for publishing the photograph. The attached sensors are the ECG sensors, the two continuous blood pressure monitors (subject's left arm), the Laser Doppler and near-infrared monitors (subject's left arm and calf), and the T-Mini sensor (head band). The PC garment (blue) is attached to the subject's lower extremities. Additional cooling garments were placed around the subjects' abdomen and lower back (not depicted).

were used synchronously to mitigate the known limitations of continuous blood pressure measurement (Pilz et al., 2022).

Peripheral perfusion

We monitored the peripheral perfusion using two different measurement approaches. The MoorVMS-LDF2 Laser Doppler (Moor Instruments, United Kingdom) was used to evaluate the peripheral blood flow and thereby vasoconstriction (Roeykens et al., 2016). The sensors were placed on the subject's forearm and upper calf.

The NIRO 200 (Hamamatsu Photonics, Japan) near-infrared spectroscopy monitor was used to determine peripheral micro perfusion by monitoring the tissue oxygenation (Hytel-Sorensen et al., 2011). The sensors were placed in close proximity to the Laser Doppler sensors on the subject's forearm and upper calf.

Brain core and forehead skin temperature (T-Mini)

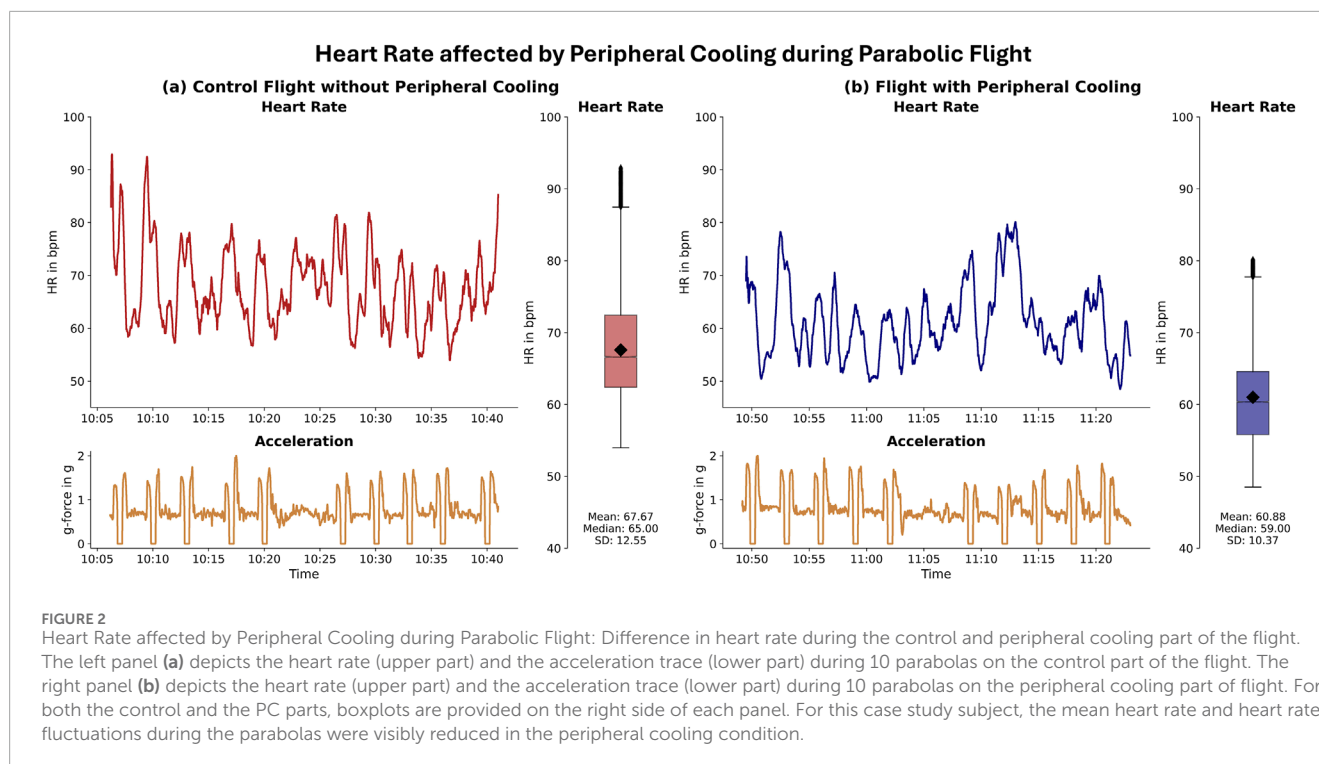
We non-invasively and continuously measured the forehead skin temperature and estimates of the core brain temperature using the T-Mini sensor (Drägerwerke, Germany). The sensor was attached to the subject's forehead and fixated using a specifically designed headband. The data were recorded using the FUM-80 data recorder (KORA Industrie-Elektronik, Germany). The setup was successfully clinically tested in a surgical application before (Soehle et al., 2020; Janke et al., 2021).

Experimental monitoring setup

The Faros ECG monitor, the SOMNOtouch NIBP and ABPMpro continuous blood pressure measurement devices, and the T-Mini core temperature sensor were attached directly to the subject. The devices were attached pre-flight and measurement was initiated as soon as the plane reached the experimental altitude before the onset of the parabolas. The MoorVMS-LDF2 Laser Doppler and NIRO 200 near-infrared spectroscopy devices were attached to an experimental rack fixated in the place. The sensors were attached to subject before the onset of the parabolas. The devices were connected to a laptop computer acting as central data recorder which was also connected to the rack. (Figure 1). Time synchronization between the devices was achieved by initializing all measurement with the data recording laptop.

Data analysis and presentation

This work is designed as a methodological feasibility and implementation case study as well as a proof-of-concept for the effectiveness of PC as a countermeasure during parabolic flight. We therefore show preliminary case study ($n = 1$) data for each measurement approach and descriptively illustrate the observed effectiveness of PC. Data synchronization was achieved by initializing all measurements with the same data recording computer. This ensured a measurement synchronization of under one second.



Ethics

Following article L. 1121-4 of the Public Health Code, this study was approved by a French Ethics Committee - Comité de Protection des Personnes Sud Méditerranée I (11/02/2022) and authorized by the French Competent Authority (04/01/2022). The experiment was conducted in agreement with the Declaration of Helsinki.

Results

Heart rate

The synchronized recording of acceleration and ECG data allows to analyse the connection between gravitational changes and changes in heart rate.

Our case study data shows apparent changes in heart rate when comparing hyper-gravity and micro-gravity conditions. Each parabola induced an increase in heart rate during the hyper-gravity phase. During the subsequent micro-gravity phase, the heart rate recovered but did not reach baseline before rising again during the second hyper-gravity phase (Figure 2).

Blood pressure monitoring

The data recorded by the Somnotouch NIBP derived continuous estimates of continuous arterial blood pressure with beat-to-beat measurement intervals. Case study data for one parabola showed a blood pressure decrease during the hyper-gravity phase, followed by a greater increase in blood pressure during the subsequent micro-gravity phase (Figure 3).

Peripheral perfusion

The Laser-Doppler measurement retrieved continuous and high-quality data of peripheral vascular flow. The data showed changes in peripheral blood flow coinciding with changes in gravitational force during the parabolas (Figure 4).

The available near-infrared spectroscopy data showed changes in tissue oxygenation during changes in gravitational force during parabolic flight (Figure 5). We experienced frequent measurement artefacts during the experiment.

Skin and brain core temperature

The temperature measurement showed stable and high-resolution recordings of both forehead skin and brain core temperature. Our data showed differences below 0.3°C in both forehead skin and brain core temperature values comparing the PC and control (Figure 6).

Discussion

One of the major challenges facing the ambitious future of human spaceflight, including reaching farther into space and incorporating a diverse astronaut corps, is to identify and validate reliable and effective countermeasures for orthostatic instability (Platts et al., 2014; Goswami et al., 2015; Lee et al., 2015; Jirak et al., 2022). The objective of this study was to evaluate PC as a potential candidate non-invasive, safe, and effective countermeasure

Continuous Blood Pressure affected by Peripheral Cooling during Parabolic Flight

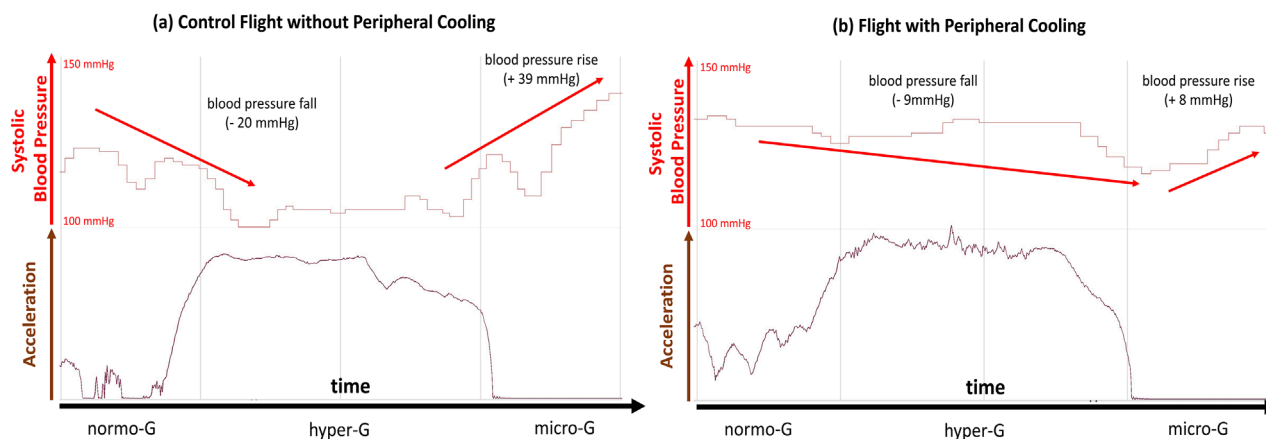


FIGURE 3

Continuous Blood Pressure affected by Peripheral Cooling during Parabolic Flight: Difference in continuous arterial blood pressure during the control and peripheral cooling flight parts of the case study subject. The left panel (a) depicts the systolic blood pressure (upper part, red) and the acceleration trace (lower part, brown) during a single parabola on the control part. The right panel (b) depicts the systolic blood pressure (upper part, red) and the acceleration trace (lower part, brown) during a single parabola on the peripheral cooling part. The baseline systolic pressure was increased during the part under peripheral cooling. Further, the blood pressure variability was visibly reduced during the peripheral cooling part, indicating a marked reduction in reaction to orthostatic challenge in the cooled condition.

Lower Extremity Blood Flow affected by Peripheral Cooling

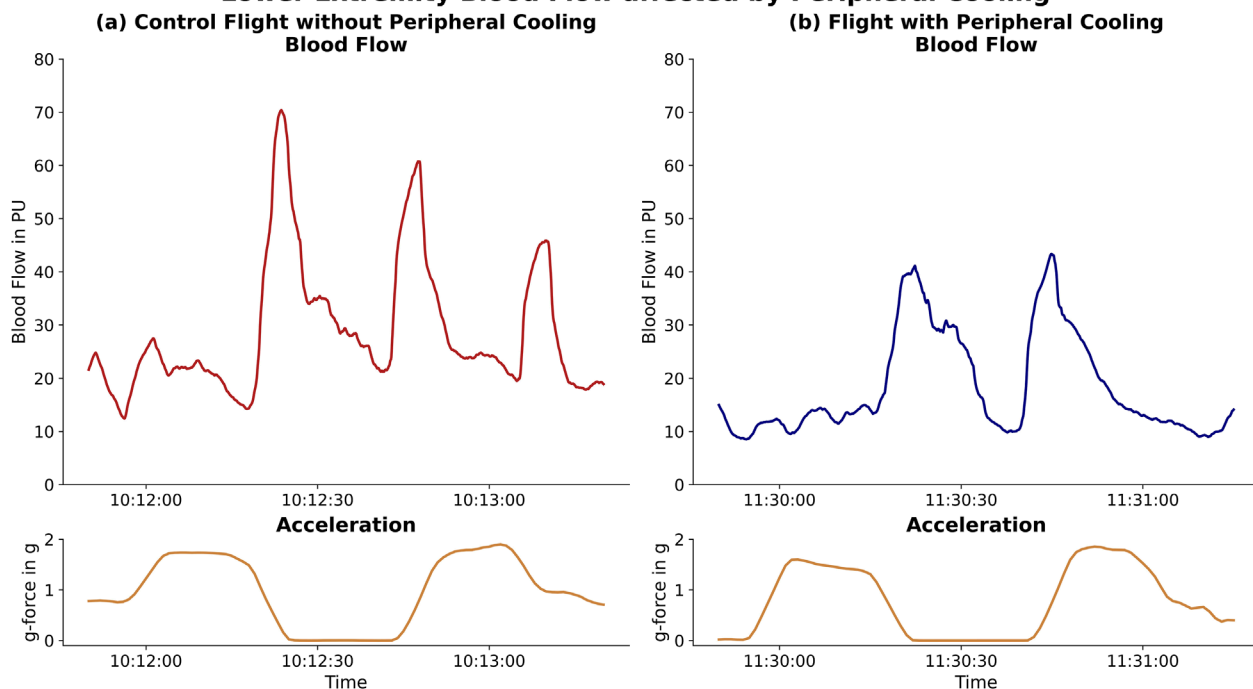
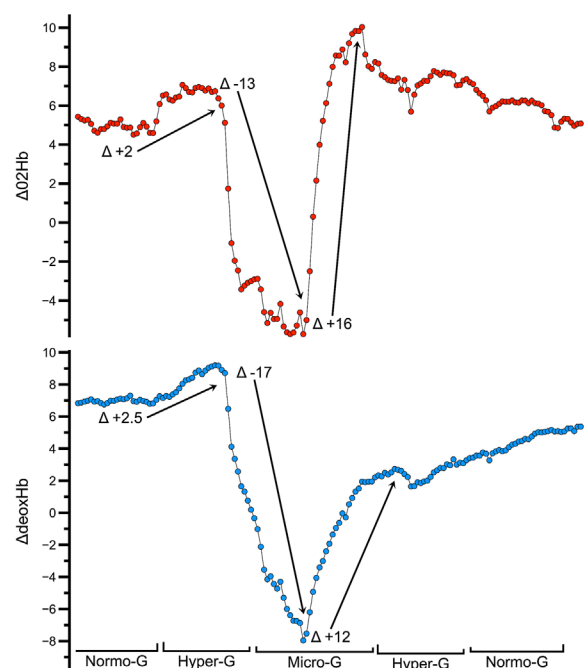


FIGURE 4

Lower Extremity Blood Flow affected by Peripheral Cooling: Difference in lower extremity blood flow during the changes in g-force (acceleration, lower panels, gold) within a parabola. The left panel [(a), red] depicts the blood flow in the control part while the right panel [(b), blue] shows the blood flow for the same subject during the cooled part. The decreased change in blood flow during the hyper-gravity phases and subsequent reduced drainage is depicted.

Peripheral Perfusion affected by Peripheral Cooling during Parabolic Flight

(a) Control Flight without Peripheral Cooling



(b) Flight with Peripheral Cooling

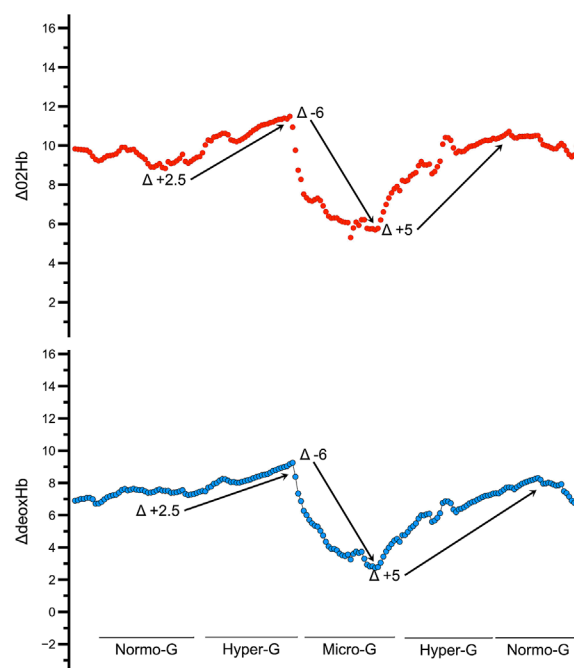


FIGURE 5

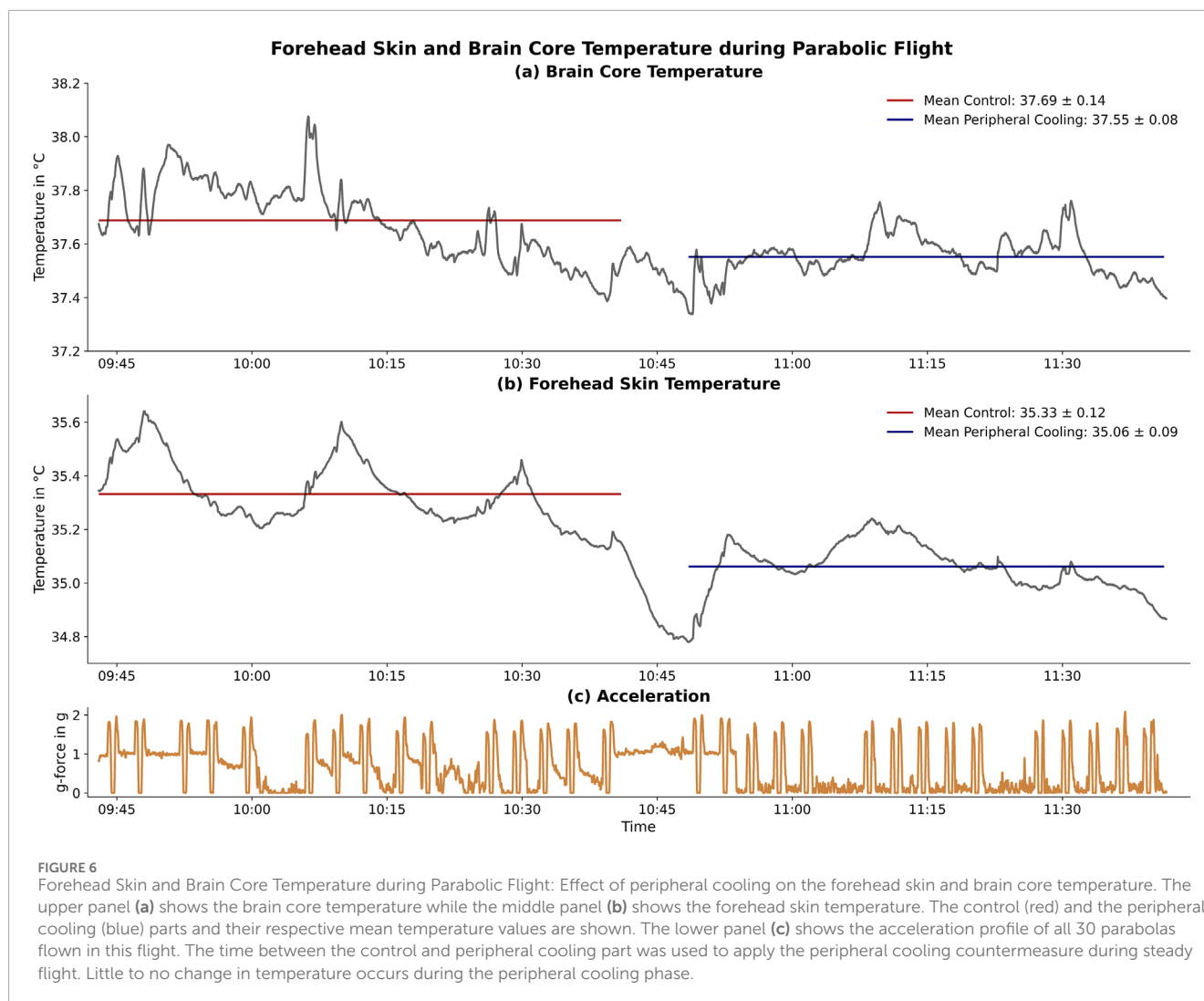
Peripheral Perfusion affected by Peripheral Cooling during Parabolic Flight: Difference in peripheral tissue oxygenation during the control and peripheral cooling flight part of the case study subject. The left panel (a) depicts the changes in oxygenated (upper part, red) and deoxygenated hemoglobin (lower part, blue) during a single parabola on the control part. The right panel (b) depicts the changes in oxygenated (upper part, red) and deoxygenated hemoglobin (lower part, blue) during a single parabola on the peripheral cooling part. Peripheral cooling visibly limits the variability of both the oxygenated and deoxygenated hemoglobin during changes in gravitational force, indicating a reduced change in perfusion during orthostatic challenge.

to orthostatic challenge during parabolic flight. This proof-of-concept highlights the feasibility of PC as a countermeasure and offers single-subject descriptive results on its effectiveness.

In recent years, various countermeasures to cardiovascular instability have been investigated, such as intravenous isotonic fluids and oral salts (Vernikos and Convertino, 1994; Cowings et al., 2015), treatment with pharmaceuticals such as Midodrine and Fludrocortisone (Ramsdell et al., 2001; Platts et al., 2004; Shi et al., 2004), compression garments (Platts et al., 2009), lower body negative pressure training (Watenpaugh et al., 2007), exposure to 1 g on a centrifuge (Moore et al., 2005; Goswami et al., 2015). However, most of these approaches suffer from either one or more severe drawbacks in regard to safety, non-invasiveness, applicability, their proven countermeasure effectiveness or their potential for long-term use. Studies have shown that while cuffs around the thighs can alleviate symptoms associated with fluid shifts, such as head congestion. But they do not significantly improve orthostatic tolerance post-flight (Robin et al., 2020). The combination of the TRPM8 activator menthol applied as a topical gel and cooling pads with low heat conductivity (carbon-gel) has not yet been studied during parabolic flight and may provide a flexible and effective alternative to existing countermeasures (Gillis et al., 2010; Shelhamer, 2016; Voronova et al., 2022).

We were able to record high-quality-high sample rate data with few artefacts—ECG, continuous blood pressure, peripheral blood flow and tissue oxygenation, preliminary impedance cardiography and skin forehead as well as brain core temperature. All measurements were non-invasive and provide high-frequency data, allowing us to analyse the effects of changes in gravitational force even in the quick changes between hyper-gravity and micro-gravity during parabolic flight. Further, the combination of used monitoring devices provided comprehensive data on changes in the cardiovascular system as well as high-quality temperature data, crucial for evaluating PC's safety and effectiveness as a countermeasure. We therefore consider the measurement paradigms and devices used in this experiment as a useful physiological measurement toolkit that can be easily applied and adapted to other physiological and extreme environment studies.

Descriptively evaluating our data for singular subjects revealed a marked effect of PC on orthostatic tolerance in all measured cardiovascular parameters. Across the bench, PC decreased measures of variability and increased overall perfusion stability while decreasing cardiovascular load. This was indicated by a decrease in mean heart rate and its variability, an increase and stabilization in blood pressure and a decrease in peripheral flow and perfusion changes between hyper-gravity and micro-gravity.



These changes are likely modulated by changes in overall autonomic nervous system reactions to parabolic flight and are beyond that influenced by individual and instantaneous factors like the breathing rate (Iwase et al., 1998; Iwase et al., 1999b).

This study is limited by its proof-of-concept and feasibility testing approach and does not represent a quantitative confirmation of the effectiveness of PC as a countermeasure. Further, research during parabolic flights is inherently limited by the short-term gravitational changes it induces, which prohibit to clearly separate whether the observed effects are fully due to the current gravitational state or lingering compensatory effects to the gravitational state just before (Shelhamer, 2016). The single-subject design does not allow for a randomization in the order of cooling and control flights, which would be needed to ensure that the effects of habituation and scopolamine are not affecting the overall results. Both sympathetic activation due to excitement as well as the effect of scopolamine, a parasympatholytic (anticholinergic) muscarinic receptor antagonist, are not expected to negatively affect the cardiovascular stability (Vybiral et al., 1990). Even small, potentially positive effects should be more pronounced in the first part of the flight (control), which further underlines the promising initial

data on peripheral cooling. In spite of these limitations, our study revealed promising single-subject data on the effectiveness of PC, showcasing a reduction in parameter variability and therefore reaction to changes in gravitational state.

Our preliminary results validate the potential of PC as a countermeasure and create an impetus for further and quantitative research into the approach if cooling as a potential cardiovascular countermeasure to gravitational stress. The peripheral cooling demonstrated in our work does not meaningfully alter core body temperature. Further, the vascular mechanisms of thermoregulation are evolutionarily developed to act for full yearly seasons. Thus, peripheral cooling could offer an attractive tool to counteract orthostatic intolerance for hours, days, or weeks after the return from space to Earth or after landing on other celestial bodies in the future.

Conclusion

This study demonstrates the feasibility of our experimental PC protocol as a cardiovascular countermeasure during parabolic flight.

The obtained physiological parameters delivered high-resolution and reliable measurement data within the challenging confines of parabolic flight. This case study data showed that PC improved the orthostatic stability across the measured physiological parameters: it decreased heart rate while both increasing and stabilizing blood pressure as well as improving peripheral flow and oxygenation stability.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Following article L. 1121-4 of the Public Health Code, this study was approved by a French Ethics Committee - Comité de Protection des Personnes Sud Méditerranée I (11/02/2022) and authorized by the French Competent Authority (04/01/2022). The experiment was conducted in agreement with the Declaration of Helsinki. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

TB: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Software, Supervision, Visualization, Writing – original draft, Writing – review and editing. VH: Writing – original draft, Writing – review and editing. NP: Writing – review and editing. LP: Writing – review and editing. AP: Writing

– original draft, Writing – review and editing. RB: Writing – review and editing. MN: Writing – original draft, Writing – review and editing. H-CG: Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Writing – original draft, Writing – review and editing. OO: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

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